STUDY ON CLINICAL PROFILE, RISK FACTORS, MORBIDITY AND MORTALITY PATTERN OF INTRA UTERINE GROWTH RESTRICTED (IUGR) BABIES ADMITTED IN SICK NEONATAL NURSERY IN A TERTIARY CARE HOSPITAL

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DECLARATION

I declare that this dissertation entitled, **STUDY ON CLINICAL PROFILE, RISK FACTORS, MORBIDITY AND MORTALITY PATTERN OF INTRA UTERINE GROWTH RESTRICTED (IUGR) BABIES ADMITTED IN SICK NEONATAL NURSERY IN TERTIARY CARE HOSPITAL** has been conducted by me at the Tirunelveli Medical College Hospital, Tirunelveli under the guidance and supervision of my Head of the Department **Dr. T. Kathir Subramaniam M.D.**, **D.C.H.,** and my unit Chief **Dr. T. Ravi Chandran M.D., D.C.H.,.** It is submitted in part fulfillment of the award of the Degree of M.D in Paediatric Medicine of the April – 2011 examination to be held under The Tamilnadu Dr. M.G.R. Medical University, Chennai. This study has not been submitted previously by me for the award of any degree or diploma from any other university.

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CERTIFICATE

Certified that this dissertation entitled **STUDY ON CLINICAL PROFILE, RISK FACTORS, MORBIDITY AND MORTALITY PATTERN OF INTRA UTERINE GROWTH RESTRICTED (IUGR) BABIES ADMITTED IN SICK NEONATAL NURSERY IN TERTIARY CARE HOSPITAL** is a bonafide work done by **Dr. T. DIANA** M.D Post graduate student of Paediatric Medicine, Tirunelveli Medical College Hospital, Tirunelveli 2008 – 2011.

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1. INTRODUCTION

Intrauterine Growth restriction (IUGR) is a common complication of pregnancy that carries significant short and long-term sequelae that reaches out to adulthood.[1] Next to preterm birth, IUGR is the second leading cause of perinatal mortality.

Intra-Uterine Growth Retardation (IUGR) is failure to attain optimal intrauterine growth which is defined as either birth weight less than the 10th percentile for gestational age or as birth weight less than 2 standard deviations below the mean value for gestational age.

When compared with normally grown fetuses after exclusion of aneuploidic and anomalous fetuses, mortality rates are increased 10-fold with perinatal mortality rates as high as 120 per 1000 for all cases of IUGR. As many as 53% of preterm stillbirths and 26% of term stillbirths are growth restricted. Up to 50% of survivors will experience intrapartum asphyxia, which adds to the already increased risk of end-organ injury.

However, the IUGR condition provides numerous challenges to both researchers of the condition and the clinician caring for the patient and includes the following: varied etiologies and definitions, altered fetal behavioral and vascular responses to IUGR, severely limited treatment options and uncertainty regarding the timing of delivery.

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2. JUSTIFICATION

Intrauterine growth restriction (IUGR) is an important clinical problem associated with increased perinatal mortality and morbidity. The neonate may be either constitutionally small or small due to pathophysiological changes with maternal, placental or fetal factors involved. A fetus with IUGR has not achieved its genetic growth potential.

Intra uterine growth-retarded babies face problems not of immaturity, but of in-utero hypoxia, poor nutrition and the resultant stress. There is a substantial overlap between their problems and those that premature babies face. The effects of this disadvantageous start, however, tend to persist. IUGR babies exhibit poor catch-up growth and impaired cognitive and neurobehavioral development. In addition, emerging evidence[2] suggests that they are also more likely than normal weight babies to suffer from degenerative diseases like hypertension, diabetes and cardiovascular diseases in adulthood.

Given the immediate and long-term implications of IUGR and its high prevalence in India, a focus on IUGR is both rational and strategic from a public health perspective. A 20% approximate prevalence of IUGR in India implies that it is a significant public health problem.[3] IUGR is strategic from the point of view of neonatal and infant mortality and adulthood morbidity. So this study attempts to find the maternal and fetal risk factors and mortality and morbidity pattern of IUGR babies admitted in a tertiary care hospital.

3. AIMS AND OBJECTIVES

The Aims and Objectives of the study are:

1) To study the Clinical profile of IUGR babies admitted in the Sick Neonatal Nursery of Tirunelveli Medical College Hospital and their Outcome during hospital stay.

2) To find out the Maternal and Fetal risk factors and their association with morbidity and mortality pattern of IUGR babies.

4. LITERATURE REVIEW

1.0 INTRODUCTION

1.1 Definitions

Intrauterine Growth Restriction

Intra-Uterine Growth Retardation (IUGR) is failure to attain optimal intrauterine growth which is defined as either birth weight less than the 10th or 5th percentile for gestational age or as birth weight less than 2 standard deviations below the mean value for gestational age. In IUGR the rate of fetal growth that is less than normal for the population and for the growth potential of a specific infant. IUGR therefore produces infants who are SGA. SGA infants can be the result of normal but slower than average rates of fetal growth, such as those constitutionally small but not abnormal infants whose parents, siblings, and more distant relatives are small.[4] SGA infants also can be the result of abnormally slow fetal growth that is caused by pathophysiologic conditions or diseases. Because growth is one of the essential features of the fetus, nearly any aberration of biologic activity in the fetus can lead to growth failure. Thus, small size at birth can be either a normal outcome or one that is a result of intrinsic or extrinsic factors that limit fetal growth potential.

Small for Gestational Age

SGA infants are classically defined as having a birth weight that is more than two standard deviations below the mean or less than the 10^{th} percentile of a population-specific birth weight vs. gestational age plot. Broader definitions include less than normal anthropometric indexes, such as length and head circumference, and marked differences between growth parameters, even when they are within the normal range.

For example, an infant can be considered "relatively" SGA when its weight is at the 25th percentile, but its length and head circumference are at the 75th percentile. In this case, the weight/length ratio (or the Ponderal index = [weight (g)]/[length (cm)]3) is less than normal, indicating that growth rates of adipose tissue and skeletal muscle, the principal determinants of weight, were less than normal.[5]

1.2 Symmetric and Asymmetric Intra Uterine Growth Restriction

IUGR can be sub-divided into two categories:

a. **Disproportional/Asymmetric or wasted IUGR:** this is characterized by a normal height and head circumference (approximates to brain growth) and low weight for height and skin fold measurements. The ponderal index (PI) for such babies is less than 2. This kind of IUGR is generally assumed to be the result of poor fetal nutrition later rather than earlier in pregnancy.
b. **Proportional/ Symmetric or stunted IUGR:** this is characterized by proportionally low weight, height and head circumference. The PI for such babies is approximately 2-2.5. This is more likely to occur if the nutritional insult occurs earlier in gestation.

Symmetric IUGR implies that brain and body growth both are limited. Asymmetric growth indicates that body growth is restricted to a much greater extent than head (and thus, brain) growth. In such cases, brain growth is considered "spared." Mechanisms that allow brain growth to continue at a faster rate than adipose tissue and skeletal muscle are not completely known. Contributing factors may include an increased rate of cerebral blood flow relative to the umbilical and systemic circulations, which has been observed in some of these infants.[6]

1.3 Prevalence of IUGR

At least 13.7 million infants are born every year at term with low birth weight (LBW), representing 11% of all newborns in developing countries. This rate is approximately 6 times higher than in developed countries. LBW, defined as < 2500 g, affects 16.4% of all newborns, or about 20.5 million infants each year. IUGR, defined as birth weight below the 10th percentile of the birth-weight-for-gestational-age reference curve, represents 23.8%, or approximately 30 million newborns per year.[7]

Very few studies in developing countries distinguish between the sub- types of LBW.[8,9] Villar and Belizan[10] have estimated that 55% of LBW in developed countries is due to prematurity on the basis of an analysis of data from 11 different regions in developed countries and 25 areas in developing countries. In developing countries they estimate that approximately 70% of the low birth weight is due to IUGR. Other studies arrive at similar estimates for India. Recent multicentric data (37000 live births) suggests that 67.2% of all LBW babies in India are IUGR.[9]

Another estimate suggested that 55% to 70% of babies in the 1501 to 2000 g category and 85% to 87% in the 2000 to 2500 g category are IUGR. According to de Onis et al approximately 20% of all Indian babies born are IUGR. This is more than two-thirds of the total LBW incidence.[3] All of these estimates are likely to be fairly conservative since home deliveries tend to get left out of such enumerations. It is worthy to note that 65.4% of deliveries in India take place at home (NFHS-2).

2.0 RISK FACTORS ASSOCIATED WITH IUGR

2.1 Fetal Causes

Fetal causes are varied and range from genetic and structural malformations to infections.

Genetic diseases

Genetic diseases of the fetus constitute 5% to 20% of causes of IUGR.[11] Chromosomal abnormalities, such as trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), trisomy 13 (Patau syndrome), and many others, can cause growth restriction presumably through the reduced number of small muscular arteries in the tertiary stem villi. Up to 16% of cases of IUGR have been associated with confined placental mosaicism. Maternal genotype is more important than fetal genotype in the overall regulation of fetal growth. However, the paternal genotype is essential for trophoblast development, which secondarily regulates fetal growth by the provision of nutrients.[12]

Fetal infections

Fetal infections are responsible for up to 10% of growth restriction cases. The TORCH [Toxoplasmosis, Other (Syphilis), Rubella, Cytomegalovirus and Herpes] organisms have been historically considered as the group to evaluate.[13] Presently, the most common causes are toxoplasmosis and cytomegalovirus in developed countries, and they should be the ones tested for most frequently. Rubella is less of a threat due to vaccination. Syphilis is still being encountered in pregnancy both in developed and developing countries. Malaria is the predominant infectious cause in Africa, South-East Asia, and other countries where malaria is endemic, accounting for 40% of cases.[14]

Multiple gestations

Multiple gestations are associated with about 3% of cases of IUGR. The risk of mortality or neonatal morbidity is higher among neonates in SGA-discordant twins than in AGA (appropriate for gestational age)-discordant twins (20% versus 6%).20 Growth restriction is a determinant of outcome in preterm discordant twins.[15]

TABLE 1 - Factors Associated with Intrauterine Growth Restriction

Fetal
Chromosomal disorders (autosomal trisomies)
Chronic fetal infections (cytomegalic inclusion disease, congenital rubella, syphilis)
Congenital anomalies—syndrome complexes
Irradiation
Multiple gestation
Pancreatic hypoplasia
Insulin deficiency
Insulin-like growth factor type I deficiency Infection (eg, CMV, toxoplasmosis, malaria, rubella)
Placental
Decreased placental weight or cellularity, or both
Decrease in surface area
Villous placentitis (bacterial, viral, parasitic)
Infarction
Tumor (chorioangioma, hydatidiform mole)
Placental separation
Twin transfusion syndrome
Maternal
Toxemia
Hypertension or renal disease, or both

Hypoxemia (high altitude, cyanotic cardiac or pulmonary disease) Malnutrition (micro- or macronutrient deficiencies) Chronic illness Sickle cell anemia Drugs (narcotics, alcohol, cigarettes, cocaine, antimetabolites) Hypertensive disorders Pregestational diabetes Autoimmune disease (eg, APS, SLE) Cardiac disease (eg, complex cyanotic congenital heart diseases) Toxic exposure (smoking, alcohol, cocaine, drugs) Malnutrition Short inter pregnancy interval
Socio demographic
Living at high altitudes Living in developing country Low socio-economic status Extremes of maternal age (less than 16 or over 35) Low socioeconomic status Low maternal weight for height Low maternal weight at her birth Maternal short stature Smoking, alcohol or drug usage

2.2 Maternal Causes

Maternal causes of IUGR are usually related to reduced uteroplacental blood flow, reduced maternal blood volume, reduced oxygen-carrying capacity, or decreased nutrition to the fetus. Often the etiology is associated with more than one of these mechanisms.

Fetal development is the product of the interaction between genetic potential and the uterine environment. The nature of this interaction is such that the achievement of inherited genetic potential is essentially mediated by the intra-uterine environment.[16] Evidence for the mediating role of the maternal environment comes from kinship studies.

According to Jane Harding[17], fetal nutrition is the end result of a precarious supply chain, of which maternal nutrition and intake during pregnancy is only the starting point. This chain can be synopsised as:

Maternal diet ➔ Maternal metabolic and endocrine status ➔Uterine blood flow ➔ Placental factors that impinge on transport and metabolism ➔ Umbilical blood flow ➔ Fetal metabolic and endocrine status.

The set of factors that could potentially influence the fetal supply line may be classified into:

(a) *Maternal nutritional factors:* maternal nutritional status can be proxied by several variables across the female lifecycle. These proxies include maternal height, pre-pregnancy weight and gestational weight gain.

(b) *Maternal non-nutritional factors:* these include parity, maternal morbidity during pregnancy including malaria and episodic illness and toxic exposures to tobacco and alcohol.

Decreased Nutrition

Because glucose drives and is essential for fetal growth, prepregnancy maternal weight and maternal weight gain in pregnancy are important variables contributing to birth weight. Thus, poor weight gain or low prepregnancy weight (associated with decreased nutrition to the fetus) can be associated with IUGR. It has been shown that protein restriction rather than caloric restriction before 26 weeks can cause symmetric IUGR. On the contrary, high protein supplementation is associated with an increase in the incidence of FGR as well as neonatal death. Gastrointestinal diseases, such as Crohn's disease, ulcerative colitis, and gastrointestinal bypass surgery, can cause

lower birth weight because of decreased nutrition to the fetus, although IUGR is not necessarily increased with these conditions.

Gestational weight gain

Gestational weight gain refers to maternal weight gain across the period of pregnancy. This can be understood either in aggregate terms or in terms of unit of weight gain per week or across the first, second and third trimesters. A WHO multi-centric study identified attained (maternal and fetal) weight at 20 weeks and at 36 weeks of gestation as a good predictor of IUGR.[18] Kramer's classic meta-analysis[8] reported a positive relationship between gestational weight gain and gestational-age-adjusted birth weight. Strauss et al.[19] in their literature review and analysis of two cohorts present substantial evidence on the importance of adequate weight gain during the second trimester of pregnancy. This remains true even when overall weight gain was adequate during pregnancy. Low weight gain in the second or third trimesters was associated with approximately double the risk of IUGR. 73% to 82% of all patients with inadequate weight gain in the second and third trimesters had normal weight gain overall. A study by Scholl et al.[20] highlights a two-fold increase in IUGR when weight gain is low in the second trimester.

Gestational weight gain is found to interact very closely with pre-pregnancy weight gain. Miller et al.[21] reported that IUGR rates increased among women with low gestational weight gain as their pre-pregnancy weight for height decreased. This implies that in developing countries with a low pre-pregnancy weight and gestational weight gain of less than 7 kg, the relative risk of poor gestational weight gain for IUGR is much higher.

The exact mechanism by which gestational weight gain affects fetal growth is not clear and it has been used largely as a rough indicator of fetal growth. Gestational weight gain is a function of (a) the physiological process of pregnancy and fetal growth i.e. plasma volume and amniotic fluid expansion, growth of uterine tissue, of the fetus and placenta etc, and (b) the laying down of fat stores. The fat stores laid down ultimately impact fetal growth rate but do not indicate the growth rate at a particular point in time.

Parity

It is correlated with birth weight such that higher parity is accompanied by an increase in mean birth weight. Kramer's meta analysis found a sample size weighted effect of 43.3 g on birth weight per birth associated with parity. It estimated a relative risk of 1.23 for IUGR associated with primi parity.[22] In the Indian context, according to the NFHS-2 an estimated 29% of births are first order births. This is indicative of the proportion of all births exposed to the risk of IUGR associated with primi parity.

Maternal morbidity

Maternal morbidity in terms of general episodic illnesses and malaria has been found to have a significant impact on the incidence of IUGR. The mechanisms by which bouts of such illnesses could impact the incidence of IUGR may be: reduction of food intake, metabolic cost of the illness and reduction in uterine blood flow.

In India the most commonly reported health problem during pregnancy is excessive fatigue. According to the NFHS-2, 43% of the respondents experienced excessive

fatigue during pregnancy. This may be linked to the fact that 35.8% of women in the reproductive age group have a body mass index of less than 18.5 kg/m2, which is indicative of chronic energy deficiency.[23]

Toxic exposures

Maternal toxic exposures through smoking or tobacco consumption and alcohol intake are found to have deleterious effects on fetal growth. Studies are unanimous regarding the effects of smoking on fetal growth. It estimated a relative risk of 2.42 for IUGR associated with smoking.[8] Cigarette smoking can affect intrauterine growth through the effects of carbonmonoxide and nicotine. Carbonmonoxide affects the supply of oxygen to the fetus while nicotine is an appetite suppressant and constricts uterine blood vessels. The effect of smoking on birth weight is more marked for the last trimester. For India, the prevalence rates for the use of smokeless tobacco by women in general vary from 0.2 % in the state of Punjab to 33.2 % in Arunachal Pradesh to 60.7% in Mizoram. However, overall prevalence of smoking and use of smokeless tobacco among women is approximately 3% and 12.4% respectively.

Alcohol consumption impacts IUGR by causing fetal hypoxia or decreasing the incorporation of amino acids from protein. Kramer found that consumption of 2 drinks or more per day decreases birth weight by 155 g. The relative risk for IUGR associated with the consumption of 2 or more drinks per day was 1.8. Exposure to absolute alcohol in the latter stages of pregnancy is found to have a relatively greater impact. Consumption of alcohol by women (above 15 yr.) in India also varies by state but at a national level is 2.2% in general and 4.4% for women of a low socio-economic status.

Teratogens

Prescription medications such as coumadin and hydantoin derivatives as well as alcohol abuse are definitely associated with certain dysmorphic features as well as impaired fetal

growth. Maternal illicit drug use will cause IUGR by its association with poor diet as well as a probable direct effect. Use of heroin40 or cocaine is associated with IUGR in 50% and 30%, respectively, of cases.

2.3 Placental Factors

The size of the placenta and its directly related nutrient transport functions are the principal regulators of nutrient supply to the fetus and thus the rate of fetal growth. Nearly all cases of IUGR are associated with a smaller-than-normal placenta.[24]

Decreased Uteroplacental Blood Flow

Maternal diseases that affect blood circulation will result in decreased uteroplacental blood flow and are to blame for the majority of IUGR cases. These diseases include hypertensive disorders (gestational and nongestational), diabetes, chronic renal disease such as renal insufficiency, systemic lupus erythematosus, antiphospholipid syndrome, and others. Acquired thrombophilias, such as anticardiolipin antibodies and lupus anticoagulant, can cause poor pregnancy outcomes such as early-onset preeclampsia and fetal demise in addition to IUGR.

Reduced Blood Volume

Women who live at high altitudes or have genetic conditions such as angiotensinogen gene mutations will have compromised placental blood flow because of reduced blood volume from poor pregnancy-associated volume expansion.

Reduced Oxygen-Carrying Capacity

Women who smoke, live at high altitudes[25], or have cyanotic heart disease, parenchymal lung disease, hemoglobinopathies, and anemias will have decreased oxygen carrying capacity which can result in IUGR. Smoking causes symmetric IUGR not only because of a reduction in oxygen-carrying capacity, but also because of impaired uterine blood flow.

At more advanced stages of placental development, placental production of growth factors and growth regulating hormones develops, leading to significant autocrine regulation of placental growth and placental regulation of fetal growth processes. Human placental lactogen is synthesized and secreted by the syncytiotrophoblast cells of the placenta.[26] Fetal growth-promoting actions of placental lactogen are mediated by stimulation of IGF production in the fetus and by increasing the availability of nutrients to fetal tissues.[27] Obviously, placental growth failure and/or nutrient deficit to the placenta can result in decreased placental production of growth factors that then would lead to fetal growth failure.

2.4 Socio-demographic factors

Maternal Age

Parity interacts with age, such that multi parity increases the risk of LBW for women aged less than 20, has little effect on women aged 20-34 and substantially decreases the risk of LBW for women more than 35 years in age. Thus the risk group from the standpoint of parity-age interaction is young multi parae.[28]

Maternal height

Evidence for the independent causal effect of maternal height on IUGR comes from Kramer's meta-analysis.[8] The meta-analysis estimated a sample size weighted effect of 7.8 g on birth weight for every centimetre of maternal height. It calculated a relative risk (RR) of 1.27 for IUGR associated with a maternal height of less than 157.5-158 cm.

For the Indian population with a mean maternal height of 152 cm and therefore an 84% prevalence of women less than 158 cm in height, the above findings imply that a maternal height of less than 158 cm may be responsible for 18% of the IUGR. The influence of maternal height on IUGR may be through a genetic mechanism or due to the physical limitations imposed on the growth of the uterus, placenta and the fetus. Maternal height is itself a function of the interaction between inherited genetic potential and the intra and extra-uterine environment. Malnutrition during uterine growth and the first two to three years of life leads to the onset of stunting which is not completely reversed even with long term exposure to good nutrition.[29] The prevention of maternal stunting appears to be a necessary element of the package of interventions required to reduce IUGR. Intervening to prevent maternal stunting would require a focus on both intra-uterine growth and development during the first two years of life. Improvement in maternal height through these interventions is essentially possible only in the long term.

Maternal pre-pregnancy weight

Maternal pre-pregnancy weight has been identified as one of the best predictors of potential IUGR.[9] Kramer's meta-analysis[8] found a sample size weighted independent

effect of 9.5 g on birth weight for every 1 kg of maternal pre-pregnancy weight. It estimated an odds ratio (OR) of 1.84 for IUGR associated with a pre-pregnancy weight of less than 49.5 kg for developed countries. For the Indian context there is some controversy about the threshold of pre-pregnancy weight below which the relative risk for IUGR is greater than 1. An Indian Council of Medical Research multicentric study recorded a pre-pregnancy weight of less than 40 kg as an influencing determinant[30] while Viller et al. found a pre-pregnancy weight of less than 45 kg as significant.[10] The mean weight of Indian women in the reproductive age group (15-49) is 46.4kg.

It has been proposed that female under nutrition across the lifecycle could harm fetal growth through its effects on maternal metabolic and endocrine status.[17] This ultimately impacts the fetus's access to nutrients. The above evidence points to the potential importance of ensuring adequate pre-pregnancy weight in the process of reducing IUGR incidence. Interventions to improve pre-pregnancy weight would imply a focus on the nutrient intake of women of the reproductive age group, with an emphasis on the period of the adolescent growth spurt.

The prevalence and effect magnitude of the factors in the Indian context may be summarised as in the following table.

Table 2: Showing Risks factors for IUGR and their prevalence in India.

Table no. 1:Risks factors for IUGR and their prevalence in India

S. No	Factors	Effect magnitude in terms of relative risk/odds ratio for IUGR[137]	Prevalence in India[138]
1.	Maternal height	RR: 1.27 for a maternal height of less than 157.5-158 cm	84%
2.	Pre-pregnancy weight	OR: 1.84 for a pre-pregnancy weight of less than 49.5 kg	The mean weight of Indian women in the 15-49 age group is 46.4 kg
3.	Gestational weight gain	RR: 1.98 for a weight gain of less than 7 kg.	Not Available
4.	Parity	RR: 1.23 for primiparity	29% first order births
5.	Maternal morbidity	Malaria control increased birth weight by 165 g	90% of the population at moderate to high risk of malaria lives in India, Indonesia, Myanmar and Thailand[139]
6.	Toxic exposures	RR: 2.42 for smoking RR: 1.78 for consumption of more than 2 drinks per day	3% of women smoke and 12.4% use smokeless tobacco. Consumption of alcohol by women nationallly is 2.2%

While each of the above factors has been found to independently affect IUGR, in interaction with each other the effects of these factors may well be greater than their independent effects.

3.0 CLINICAL PROBLEMS / OUTCOMES OF THE SMALL FOR GESTATIONAL AGE NEONATE

Mortality

The consequences of small size for gestational age depend on the etiology, severity, and duration of growth restriction. There continues to be much debate on this subject. By now, many studies have been conducted over extended periods of changing perinatal management and increasing survival rates of smaller, more preterm infants, many of whom have been classified differently at different times and among different studies regarding their degree of IUGR. Some studies have indicated that the fetus responds to the “stress” of growth restriction with an acceleration of maturity, which

ultimately is protective for the infant. Others have found no evidence of improved survival after perinatal stress, and SGA status has been shown to be an independent predictor of increased fetal, perinatal, and neonatal death.[31] On balance, there is little evidence to support the concept of improved survival after perinatal stress in SGA infants, and the perinatal mortality rate for SGA infants with relatively severe IUGR is 5 to 20 times that of AGA infants of the same gestational age.[32] Particularly when adjusted for maternal neonatal risk factors of IUGR, including birth weight percentile, gestational age at birth, maternal height, prepregnancy weight, gestational weight gain, race, and parity, a subgroup of SGA infants is defined that has consistently and markedly higher perinatal mortality and morbidity rates than normally grown infants.[33]

Asphyxia

SGA infants frequently do not tolerate labor and vaginal delivery, and signs of fetal distress are common. In such cases, the already stressed, chronically hypoxic infant is exposed to the acute stress of diminished blood flow during uterine contractions. Cord blood lactate concentrations are often increased despite overall normal cord blood pH. Preterm SGA infants are delivered by cesarean section twice as often as preterm AGA infants.[34] SGA infants have an increased incidence of low Apgar scores at all gestational ages, and these infants frequently need resuscitation. The acute fetal hypoxia, acidosis, and cerebral depression may result in fetal death or neonatal asphyxia. Sequelae of perinatal asphyxia includes hypoxic-ischemic encephalopathy, heart failure from hypoxia-ischemia and glycogen depletion, meconium aspiration syndrome, persistent pulmonary hypertension, gastrointestinal hypoperistalsis and ischemia- induced necrosis leading to focal perforation, and acute renal tubular necrosis and renal failure.

Hypoglycemia

Hypoglycemia is extremely common in SGA infants, increasing with the severity of IUGR. The risk of hypoglycemia is greatest during the first 3 days of life, but fasting hypoglycemia, with or without ketonemia, can occur repeatedly up to weeks after birth. Early hypoglycemia usually is as a result of diminished hepatic and skeletal muscle glycogen contents.[35] Early hypoglycemia is aggravated by diminished alternative energy substrates, including reduced concentrations of fatty acids from the scant adipose tissue and decreased concentrations of lactate from the hypoglycemia. Hyper-insulinemia, increased sensitivity to insulin, or both may contribute to a greater incidence of hypoglycemia, although there are very few, if any, accurate measures of insulin sensitivity at different times and among different conditions in SGA infants to support such assumptions.

SGA infants also demonstrate decreased gluconeogenesis, and resolution of persistent hypoglycemia is coincident with improved capacity for, and rates of, gluconeogenesis. Deficient counter regulatory hormones also contribute to the pathogenesis of hypoglycemia in SGA infants.[36] Catecholamine release is deficient in these neonates during periods of hypoglycemia. Although basal glucagon levels may be elevated, exogenous administration of glucagon fails to enhance glycemia because of the decreased hepatic glycogen stores.

Hyperglycemia

Very preterm SGA infants have developmentally low insulin secretion rates and plasma insulin concentrations, which may underlie the relatively common problem of hyperglycemia in ELBW SGA infants.[37] Higher concentrations of Counter regulatory

hormones, such as epinephrine, glucagon, and cortisol, also may contribute, although there is only limited evidence to support this commonly held assumption. In contrast, administration of insulin to even preterm SGA infants usually produces prompt decreases in glucose concentration, indicating at least normal and probably greater than normal insulin sensitivity.[38]

Nutritional Problems

A rapid rate of glucose supply can lead to marked hyperglycemia, especially in the ELBW preterm SGA infant. On the other hand, amino acid intolerance is not exaggerated in SGA infants, despite some earlier evidence that amino acids are not used as readily for gluconeogenesis. If insulin and IGF-I are deficient in these infants, one would also expect lower anabolic rates until glucose and amino acid supplies and concentrations, and production rates of these growth factors, are restored. Similar issues may apply to lipid tolerance. Such considerations have prompted some reluctance to feed the SGA infant as aggressively as their deprived nutritional state would indicate, but large-scale, rigorous trials of different rates and amounts of nutrition to such infants have not been conducted. Such trials are needed to determine whether these infants will tolerate more aggressive feeding and whether this will result, safely, in improved nutritional rehabilitation, growth, and perhaps, neuro developmental outcome.

Temperature Regulation

Compared with term infants, SGA infants have a narrow thermo neutral range. Heat production cannot match the rate of heat loss with continued cold stress. The rapid heat loss as a result of the large head-to-body ratio and increased surface area seen in all infants is exaggerated in the SGA infant. Heat is also lost more quickly through a

thin layer of subcutaneous fat insulation. Because they are gestationally more mature than their preterm peers, SGA infants do have a more generous thermo neutral range for weight and are better able to maintain the increased metabolic rate necessary to increase heat production.[39] Heat production may be impaired by concurrent conditions of hypoglycemia and hypoxia seen commonly in these patients. The normal response to cold involves increased muscular activity and catecholamine (nor epinephrine) release. Central nervous system depression may prevent this normal response to cold.[40]

Polycythemia

SGA infants manifest an increased incidence of polycythemia. Increased red blood cell volume is likely related to chronic in utero hypoxia leading to increased erythropoiesis. Maternal-fetal transfusion may occur chronically with fetal hypoxia or more acutely with episodes of fetal distress. Even when not polycythemic (venous hematocrit greater than 60), SGA infants have higher than normal hematocrit. Approximately half of all term SGA infants have a central hematocrit above 60% and about 17% of term SGA infants have a central hematocrit above 65% in contrast to only about 5% in AGA term infants.[41] Most polycythemic infants remain asymptomatic, but SGA infants are at greater risk of symptoms and clinical consequence. Interestingly, male SGA infants are at highest risk. Polycythemia contributes to hypoglycemia and hypoxia. Altered viscosity interferes with neonatal hemodynamics and results in abnormal postnatal cardiopulmonary and metabolic adaptation.

Infections

Immunologic function of SGA infants may be depressed at birth and may persist into childhood, as in older infants with postnatal onset of malnutrition.[42] Deficiencies have been demonstrated in lymphocyte number and function, which include decreased spontaneous mitogenesis and reduced response to phytohemagglutinin. Similarly, these infants tend to have lower immunoglobulin levels during infancy and demonstrate an attenuated antibody response to oral polio vaccine.

Miscellaneous Problems

At birth, cord prealbumin and bone mineral content are low in term SGA infants.[43] Calcium and iron stores may be low as a result of chronic decreased placental blood flow and insufficient nutrient supply. Significant **hypocalcemia** can occur after stressful birth complicated by acidosis. **Thrombocytopenia, neutropenia,** prolonged thrombin and partial thromboplastin times, and elevated fibrin degradation products are also problems among SGA infants.[44] Sudden infant death syndrome may be more common after IUGR. Inguinal hernias also disproportionally follow preterm IUGR.

TABLE 3. SUMMARY OF CLINICAL PROBLEMS OF THE SMALL- FOR GESTATIONAL- AGE NEONATE

Problem	**Pathogenesis/ Pathophysiology**	**Prevention/ Treatment**
Intrauterine death	Chronic hypoxia Placental insufficiency Growth failure Malformation Infection Infarction/abruption Preeclampsia	Antenatal surveillance Fetal growth by ultrasound Biophysical profile Doppler velocimetry Maternal treatment: Bedrest, O2 Delivery for severe/worsening fetal distress
Perinatal Asphyxia	Acute hypoxia/abruption Chronic hypoxia Placental insufficiency/Preeclampsia Acidosis Glycogen depletion	Antepartum/intrapartum monitoring Adequate neonatal resuscitation

Meconium Aspiration	Hypoxia	Resuscitation including tracheal suctioning for aspiration
Hypothermia	Cold stress Hypoxia Hypoglycemia Decreased fat stores Decreased subcutaneous insulation Increased surface area Catecholamine depletion	Protect against increased heat loss Dry infant – Radiant warmer, Hat Thermo neutral environment Nutritional support
Persistent pulmonary hypertension	Chronic hypoxia	Cardiovascular support Mechanical ventilation, Nitric oxide
Hypoglycemia	Decreased hepatic/muscle glycogen Decreased alternative energy sources Heat loss; Hypoxia Decreased gluconeogenesis Decreased counter regulatory hormones Increased insulin sensitivity	Frequent measurement of blood glucose Early intravenous glucose support
Hyperglycemia	Low insulin secretion rate Excessive glucose delivery Increased catecholamine	Glucose monitoring Glucose infusion <10 mg/min/kg Insulin administration
Polycythemia	Chronic hypoxia Maternal-fetal transfusion Increased erythropoiesis	Glucose, oxygen Partial volume exchange transfusion
Acute renal failure	Hypoxia/ischemia	Cardiovascular support
Immunodeficiency	Malnutrition Congenital infection	Early, optimal nutrition Specific antibiotic and immune therapy

4.4 IMPLICATIONS OF IUGR

IUGR and mortality and morbidity

Ashworth[45] reviewed 29 data sets to assess the risks of mortality and morbidity associated with IUGR. He estimated that for term infants66 weighing between 2000 and 2499 g the risk of neonatal death is four times higher than that for infants weighing between 2500 and 2999 g. Infants weighing between 2000 and 2499 g have a ten times higher risk of dying in the neonatal period than those weighing between 3000 and 3499 g. Ashworth presents data from 9 studies substantiating the observation that IUGR infants are more susceptible to diarrheal diseases and

respiratory tract infections. The studies indicate that IUGR infants are between 1.2 and 3.6 times more likely to develop these infections.

IUGR and physical development

IUGR infants are found to be much more likely to exhibit growth deficiencies, which appear to be permanent. A study in Guatemala compared development at age 3 for children born with disproportional IUGR, proportional IUGR and those born normal (control). The study found that the group with disproportional IUGR recuperated from thinness within the first few months. However infants with proportional IUGR remained lighter and shorter and had a smaller head circumference than the infants in the other two groups.[10]

An Indian study by Bhargava et al.[30] followed up small for date infants with a birth weight of 2000 g for 6 years and found significant growth retardation in comparison with children of the same age born with normal weight. They also displayed delayed skeletal growth and maturation between 6-10 years of age and impaired immune competence.

However, the low socio-economic status of these children and the resultant lack of stimulation and opportunity to learn could have confounded these results. To avoid such a bias, Proos et al.[46] studied growth and development of Indian children adopted in Sweden. 81% of these children, adopted in early infancy, were IUGR. They found significant differences with respect to height for age and weight for age at 2 years between children < 2000 g at birth and those > 2000 g at birth. This indicates that the effects of IUGR cannot be reversed by an ideal environment and postnatal nutrition.

Strauss and Dietz[19] also found a significant growth difference in terms of height and weight in their study. Strauss and Dietz compared 220 IUGR children with their normal birth weight siblings, thereby controlling for confounders like genetic potential and environmental factors. While IUGR infants as a group tend to be shorter than their appropriate birth weight counterparts, they do exhibit partial catch up growth during the first two years of life.[47]

IUGR and cognitive development

Subtle neuro cognitive deficiencies are found to be common in IUGR babies. Evidence from the Child Development Centre, Kerala[48] shows that for IUGR babies, every 500g decrease in birth weight is associated with a corresponding decrease in the developmental status at one, two and five years of age. In the Guatemalan study, described above, Villar et al.[10] found that children born with proportional IUGR obtained a lower IQ score at 3 years on the Composite Infant Scale as compared to children with disproportional IUGR who in turn scored lower than the control group.

IUGR and adult morbidity: *The Fetal Origins of Adult Disease*

The Barker Hypothesis[2] states that many degenerative diseases in adults, such as Coronary Heart Disease (CHD), hypertension, stroke and Non Insulin Dependent Diabetes Mellitus (NIDDM) are induced by the effects of under nutrition in fetal life and infancy, reflected as Low Birth Weight. This is explained by the effect of fetal "programming". Fetal programming refers to the process wherein in-utero exposure to under nutrition leads to permanent changes in metabolic and hormonal regulation systems in the body.

Nevertheless, at the end of the First World Congress a BMJ editorial[49] commented that the evidence looked convincing, especially for the association between IUGR and blood pressure and non insulin dependent diabetes mellitus. The combined evidence therefore predicts that more heart disease and impaired glucose tolerance will be seen in India.

This study was aimed at finding out the immediate outcome of IUGR babies and Risk factors associated with IUGR and its outcome.

5. MATERIALS AND METHODS

Study Design:

This is a Cross Sectional study.

Place of study:

This study was carried out in the Department of Pediatrics, Neonatal Unit, Tirunelveli Medical College Hospital.

Study period:

This study was carried out between November 2008 and October 2010.

Sample size

According to the following sample size calculation formula, 120 IUGR babies were included in the study.

Sample size **(n) = 4pq/d2** **[**p = prevalence. q= 1-p d= error allowed (25% of p)]

For the prevalence of 35%, sample size will be 119; for the prevalence is 40%, sample size will be 96. So, based on the prevalence of 35%, 120 were included in this study.

Inclusion Criteria

- Newborns with IUGR defined by Birth weight less than 10^{th} percentile (Annexure: 2) and Ponderal Index admitted in the SNN ward of Tirunelveli Medical College Hospital.

Exclusion Criteria

- Newborns with chromosomal abnormalities.
- Newborns with congenital anomalies.

METHOD OF DATA COLLECTION

Among all the IUGR babies admitted in SNN during the above study period, the 120 babies who satisfied the Inclusion criteria were selected by systematic random sampling. Informed consent of their parents was taken after explaining in detail about the method and procedures involved in the study in their vernacular language.

The socio demographic profile and relevant information of individual babies and their respective mothers were collected by interviewing the mother using a structured proforma (Annexure: 1). The clinical details, complications and outcome at discharge were noted down. The following investigations were carried out for all the babies under study.

Laboratory Investigation:

1) CBC – Hb, PCV, TC, DC, Platelet Count, ESR
2) Blood Sugar, Urea and Serum Creatinine
3) Serum calcium
4) Chest X Ray
5) Total and Direct Bilirubin (Only for Icteric babies)
6) Sepsis Screening (Only for the suspected sepsis babies) - Peripheral smear for band forms and Toxic granules, Blood culture and sensitivity, CSF Analysis with culture and sensitivity.

a) Hb: Hemoglobin less than 13 mg/dl was considered as Anemia.

b) PCV: The value of PCV more than 65% was taken as Polycythemia.

c) Total WBC count: A total count of < 5,000/cu.mm or >20,000/cu.mm was taken as abnormal and considered as suspicious of sepsis.

d) Differential count: Differential count was considered mainly to find out Neutropenia which is indicative of sepsis. Absolute Neutrophil count less than 2000 was considered as Neutropenia.

e) Platelet Count: Platelet count less than 1,00,000 was considered as Thrombocytopenia.

f) ESR: Micro ESR value more than 15mm at one hour was considered as sepsis.

g) Blood Sugar: Blood sugar value less than 45 mg/dl in one or more occasions were considered as hypoglycemia.

h) Blood Urea and Serum Creatinine: Value of Blood urea more than 40mg/dl associated with the value of Serum Creatinine more than 1mg/dl was considered as acute renal failure.

i) Serum calcium: Serum Calcium less than 7mg/dl was considered as hypocalcaemia.

j) Chest X- Ray: Chest X-ray was done in all babies .

k) Total and Direct Bilirubin: The Total and Direct Bilirubin were taken for only the clinical icteric babies and categorized as having hyperbillirubinaemia based on Bilirubin Nomogram.

l) Peripheral smear for band forms and Toxic granules: Presence of band forms and toxic granules in peripheral smear study was considered as abnormal and considered as sepsis.

m) Blood culture and sensitivity: Blood culture and sensitivity test was done only in the cases of suspected sepsis. For the blood culture, 1ml of blood was drawn form a peripheral vein. This was then incubated at $37^{o}C$ under aerobic condition and subculture was made on Mac Conkey agar media after 24 hrs of incubation. If any growth occurred at 48 hrs, it was again subcultured in Mac Conkey agar. Cultures were taken as sterile if no growth occurred at 96 hrs. Anaerobic cultures were not done.

n) CSF analysis and culture: CSF analysis also was done only in the cases of suspected sepsis. CSF was obtained by lumbar puncture performed aseptically with a 24 gauze disposable needle. Sample was transported promptly to the laboratory for analysis and culture and sensitivity.

OUTCOME MEASURES

The following outcome measures were quantified in the study.

1) Immediate Complications.
2) Condition at discharge.
3) Risk factors associated with IUGR – Maternal
4) Risk factors associated with IUGR – Fetal.

Maternal Risk factors:

The socio- demographic and antenatal characteristics of the mothers were analysed and the following maternal risk factors associated with IUGR were considered in this study. They are

- Lower age (≤ 25) (mean)
- Rural residence
- Lower Education (≤ Primary school)
- Lower Income (Monthly family income ≤ Rs. 3000) (mean)
- Anemia (Hb ≤ 10mg/dl)
- Lower Weight gain (≤ 10 kg)
- Malnutrition (Pre-pregnancy BMI ≤ 18.5)
- Multiple Gestations
- Heart Disease (RHD, CHD)
- Pulmonary Disease (Bronchial asthma, COPD)
- Pregnancy Induced Hypertension (BP >140/90 mm Hg)
- Diabetes Mellitus (by History)
- Tobacco Use (Using tobacco more than 2 yrs)
- Long Infertility (Infertility > 8 yrs) and
- UTI (from ANC record).

Fetal Risk Factors:

The fetal risk factors considered for analysis of this study were

- Gender of the baby
- Weight

- Gestational Age (by LMP and New Ballard scoring – Annexure 3)
- Asymmetrical IUGR (Ponderal Index ≤ 2) [Ponderal Index = Weight in gm / {Legnth in cm}^{3} x 100] and
- Mode of Delivery.

Immediate Complications*:

The important immediate complications considered were:

- **Metabolic:** Hypoglycemia and Hypocalcaemia
- **Hematological:** Neutropenia, Polycythemia, Anemia and Thrombocytopenia
- **Organ Dysfunction:** Acute Renal Failure, Perinatal Asphyxia, Meconium Aspiration, Pulmonary Hemorrhage, Persistent Pulmonary Hypertension and Respiratory Distress Syndrome.
- **Infection/ Others:** Sepsis, Meningitis, Hypothermia and Hyperbillirubinaemia.

Perinatal Asphyxia was considered when Apgar score was ≤ 3 at 5 minutes and requiring bag and mask ventilation; seizures within 24 - 48 hrs after birth in asphyxiated babies. The staging was done using Sarnat and Sarnat stages[50] of Hypoxic Ischemic Encephalopathy (Annexure: 4).

Meconium Aspiration syndrome was considered in babies born with meconium stained amniotic fluid associated with early onset respiratory distress (defined by Downes scoring) with poor lung compliance and hypoxemia with characteristic radiographic features in lungs (hyperinflation of lung fields with flattened diaphragms and coarse irregular patchy infiltrates).

* Definitions and reference values are based on NEONATOLOGY Management, Procedures, On-call Problems, Diseases and Drugs by Tricia lacy Gomela, Mc Graw Hill Lange International Edition – 6th Edition.

Pulmonary Hemorrhage was diagnosed by gross bloody secretions in the Endo Tracheal tube accompanied by respiratory decompensation requiring increased respiratory support.

Persistent Pulmonary Hypertension was diagnosed by cyanosis with severe illness by clinical exam and prominent precordial impulse, loud S2 with single/ narrowly split and/ or a systolic murmur consistent with tricuspid regurgitation by cardiac examination and pre and posductal difference in oxygen saturation ≥ 10% in the absence of structural heart disease and confirmed by echocardiography.

Respiratory Distress Syndrome was considered in preterm babies presenting with respiratory difficulty including tachypnoea (> 60 breaths/ minute), chest retractions with or without grunting, cyanosis in room air that persisted or progressed over the first 48 -96 hours of life with the characteristic chest radiography (uniform reticulo-granular pattern and peripheral air bronchograms).

Hypothermia was considered when axillary temperature < 36.5^0C.

CLINICAL OUTCOME:

It was assessed in three aspects namely Dead, Abnormal neurological examination at discharge and Good condition at discharge. Babies who had some morbidity but improved clinically over the duration of stay in the hospital and taking feeds properly during discharge were categorized as discharged with good condition. Babies having poor feeding & sent along with antiepileptic drugs and showing abnormal neurological examination were categorized as Abnormal neurological examination at discharge.

Abnormal neurological examination includes:

- asymmetries of posture or reflexes (marked or persistent)
- decreased flexor or extremity tone or axial tone for post conceptional age
- cranial nerve or oromotor dysfunction
- abnormal sensory responses
- abnormal behaviour (lethargy, irritability or jitteriness) and
- extensor neck, trunk or extremity tone.

(Amiel Tison angles – Annexure: 5)

Statistical Methods:

Data were entered in Excel spreadsheet and analysed using SPSS version 13.0. The results were analysed using the statistical test like simple proportions, Risk ratio and Chi-square test. The p- value < 0.05 was considered as statistically significant

6. OBSERVATIONS AND RESULTS

1.0 General Characteristics

1.1 Gender Distribution

Gender	Number	Percent
Male	65	54.2
Female	55	45.8
Total	120	100

Among the total study population of 120 IUGR babies, 65 (54.2%) are males and 55 (45.8%) are females.

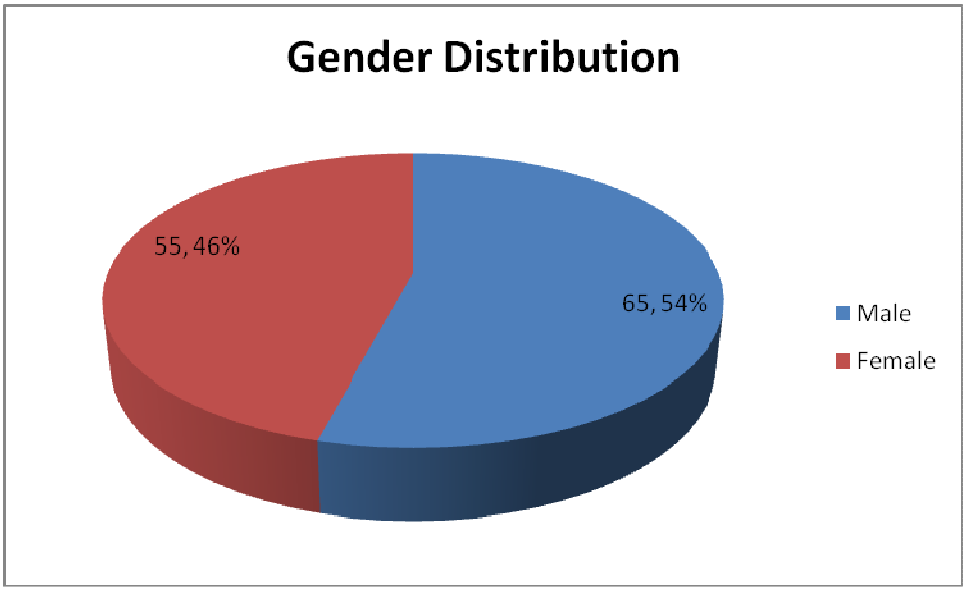

Fig 1.1 Showing the Gender distribution of the study population

1.2 Mothers – Distribution by Gravida

Gravida	Number	Percent
Primi	82	68.3
2nd Gravida	28	23.3
3rd Gravida	8	6.7
4th Gravida	2	1.7
Total	120	100

The above table shows the gestational age of the respective mothers of the study population. 82 (68.3%) mothers are primi and 28 (23.3%) are 2nd gravida mothers. The 3rd gravida mothers are 8 (6.7%) and only 2 (1.7%) are the 4th gravida mothers.

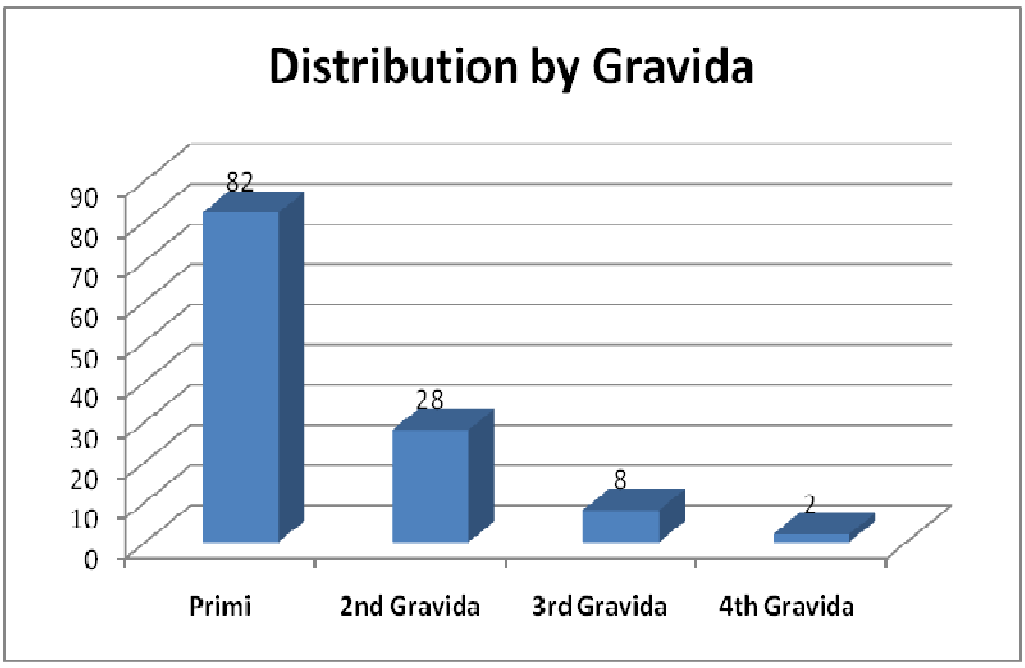

Fig 1.2 Showing distribution of Mothers by Gravida

1.3 Mode of Delivery

Mode of Delivery	Number	Percent
Normal Vaginal	72	60.0
Assisted	10	8.3
LSCS	38	31.7
Total	120	100

Of the 120 babies, 72 (60.0%) have been delivered by normal vaginal delivery and 10 (8.3%) have been delivered by Assisted delivery. 38 (31.7%) have been delivered by Caesarian section.

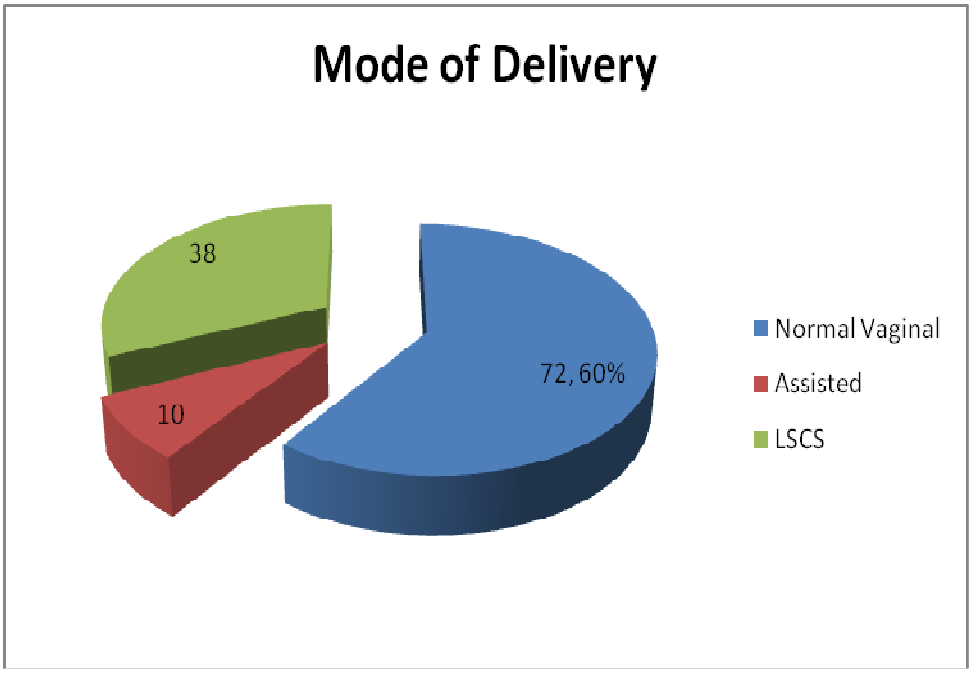

Fig 1.3 Pie Diagram showing the Mode of Delivery

1.4 Distribution by Gestational Age

Gestational Age	Number	Percent
Preterm	22	18.3
Term	98	81.7
Total	120	100

Of the total 120 babies 22 (18.3%) are Preterm babies and 98 (81.7%) are Term babies.

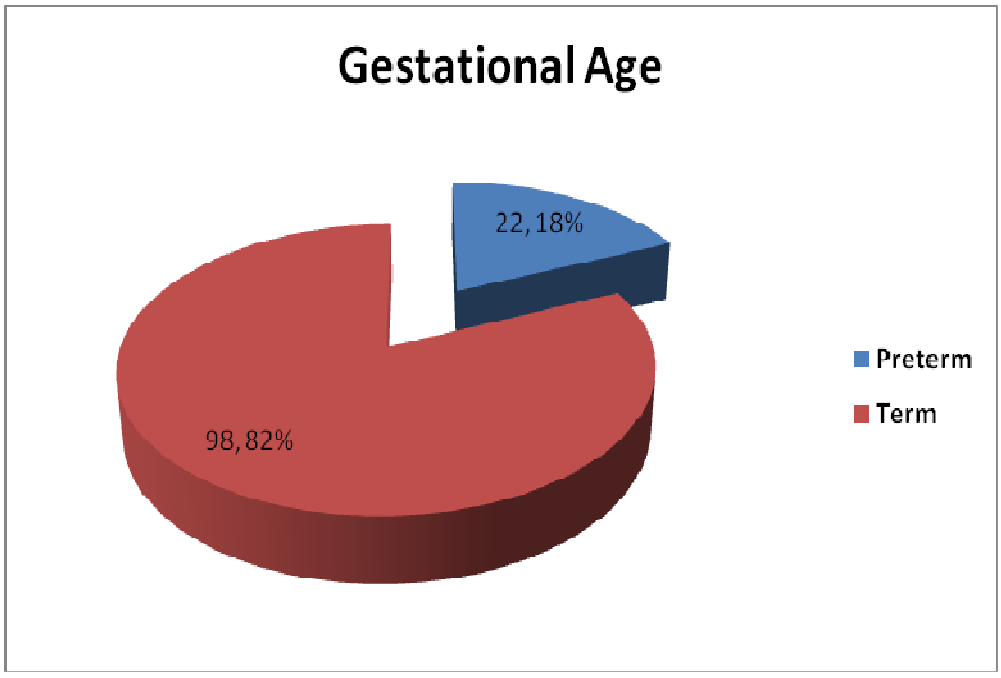

Fig 1.4 Pie diagram showing proportion of Preterm

1.5 Distribution by Birth Weight

Birth Weight	Number	Percent
< 1000 gm	6	5.0
1000 – 1499 gm	10	8.3
1500 – 1999 gm	38	31.7
2000 – 2500 gm	66	55.0
Total	120	100

Of the 120 babies 66 (55.0%) are in the birth weight category of 2.0 - 2.5 kg and 38 (31.7%) are in the birth weight category of 1.5 – 2.0 kg. 10 (8.3%) babies are in the category of 1.0 – 1.5 kg and 6 (5.0%) babies are in less than 1.0 kg category.

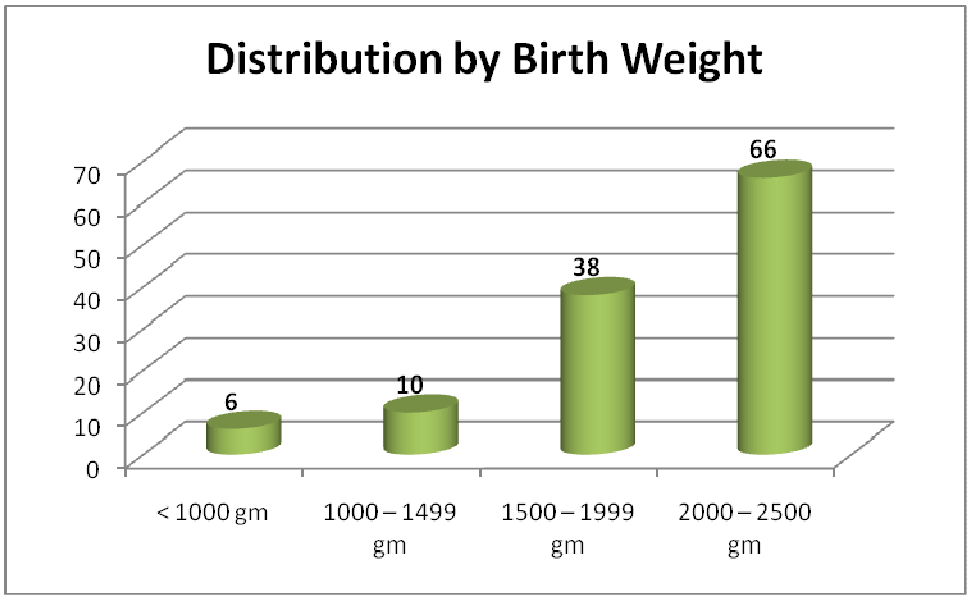

Fig 1.5 Bar Diagram showing distribution of Birth Weight

1.6 Distribution of IUGR by Ponderal Index

Ponderal Index Group	Number	Percent
Asymmetrical (PI ≤ 2)	82	68.3
Symmetrical (PI > 2)	38	31.7
Total	120	100

Among the 120 study population 82 (68.3%) babies were classified as asymmetrical IUGR and 38 (31.7%) babies were classified as symmetrical IUGR as per Ponderal Index.

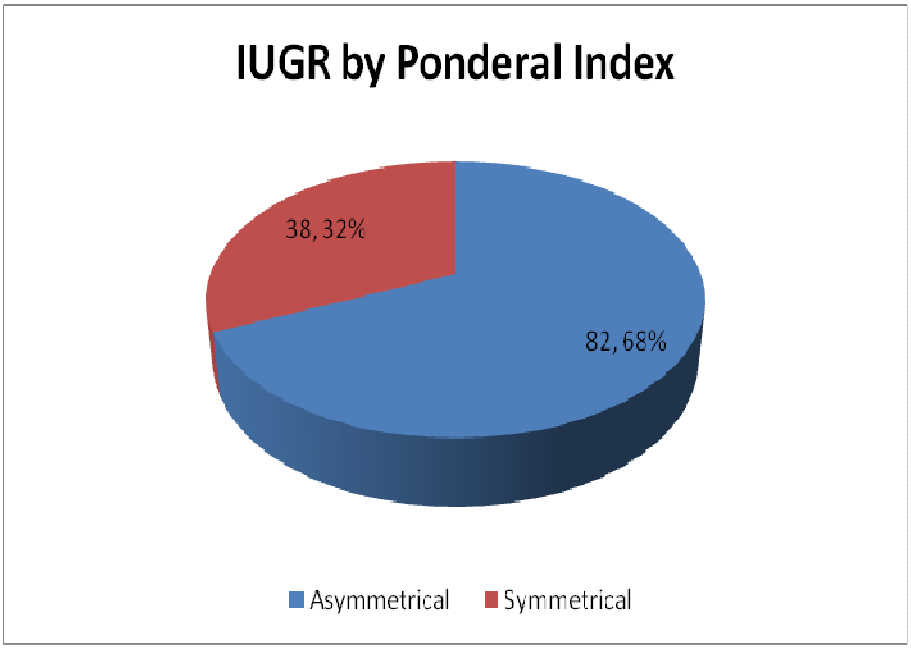

Fig 1.6 Pie diagram showing distribution of IUGR by Ponderal Index

2.0 Morbidity and Mortality Pattern of IUGR

2.1 Morbidity Pattern of IUGR

Complications	Number	Percent
Metabolic		
Hypoglycemia	76	63.3
Hyperglycemia	10	8.3
Hypocalcaemia	36	30.0
Hematological		
Neutropenia	6	5.0
Polycythemia	6	5.0
Anemia	24	20.0
Thrombocytopenia	30	25.0
Organ Dysfunction		
Acute Renal Failure	22	18.3
Perinatal Asphyxia	54	45.0
Meconium Aspiration	20	16.7
Pulmonary Hemorrhage	6	5.0
Persistent Pulmonary Hypertension	4	3.3
Infection/ Others		
Sepsis	40	33.3
Meningitis	6	5.0
Hypothermia	34	28.3
Hyperbillirubinaemia	20	16.7

The above table shows that hypoglycemia (63.3%) and Perinatal Asphyxia (45.0%) are the commonest complication. Other commoner are Sepsis (33.3%), hypocalcaemia (30.0%), hypothermia (28.3%) and thrombocytopenia (25.0%).

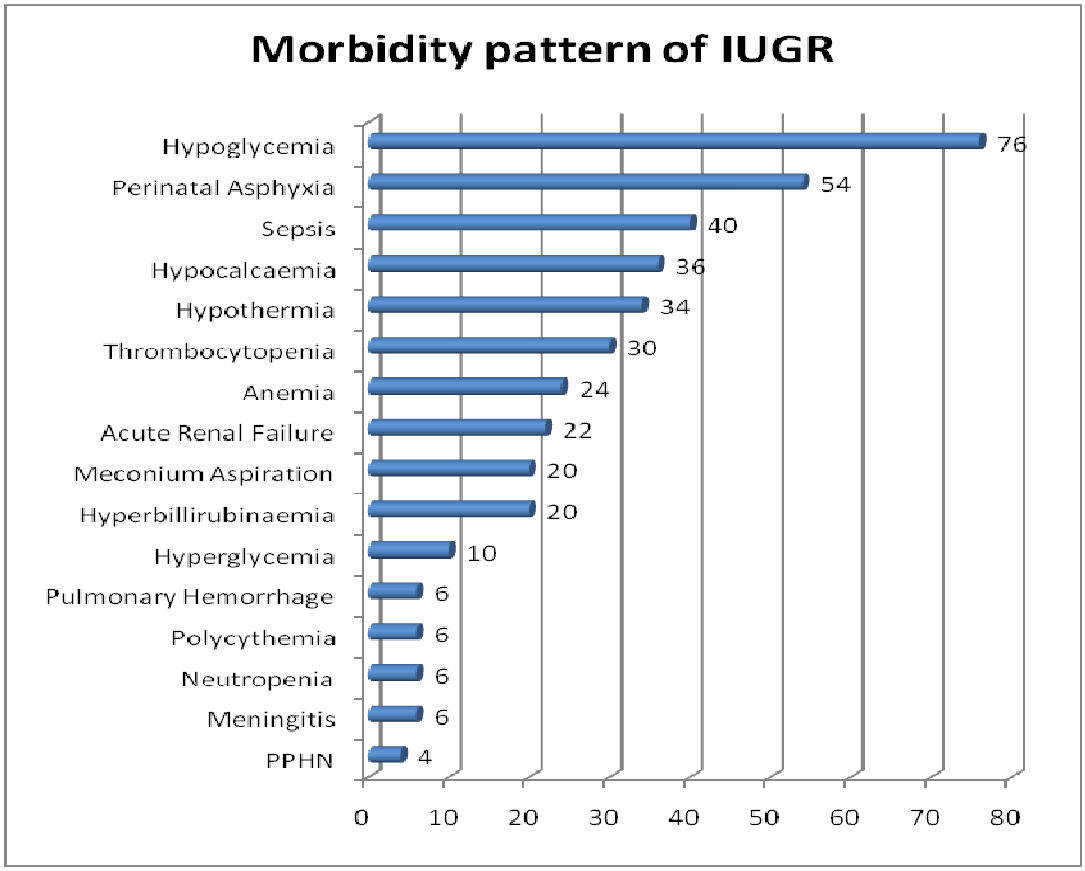

Fig 2.1 Bar Diagram showing complications of IUGR

2.2 Respiratory Distress Syndrome in Preterm (N= 22)

RDS	Number	Percent
Yes	7	31.8
No	12	68.2
Total	22	100

Among the total 22 preterm babies 7 (31.8%) babies have Respiratory Distress Syndrome.

2.3 Mortality in IUGR

	Number	Percent
Dead	22	18.3
Discharged	98	81.7
Total	120	100

Of the 120 IUGR babies 22 (18.3%) have died at hospital and 98 (81.7%) have been discharged.

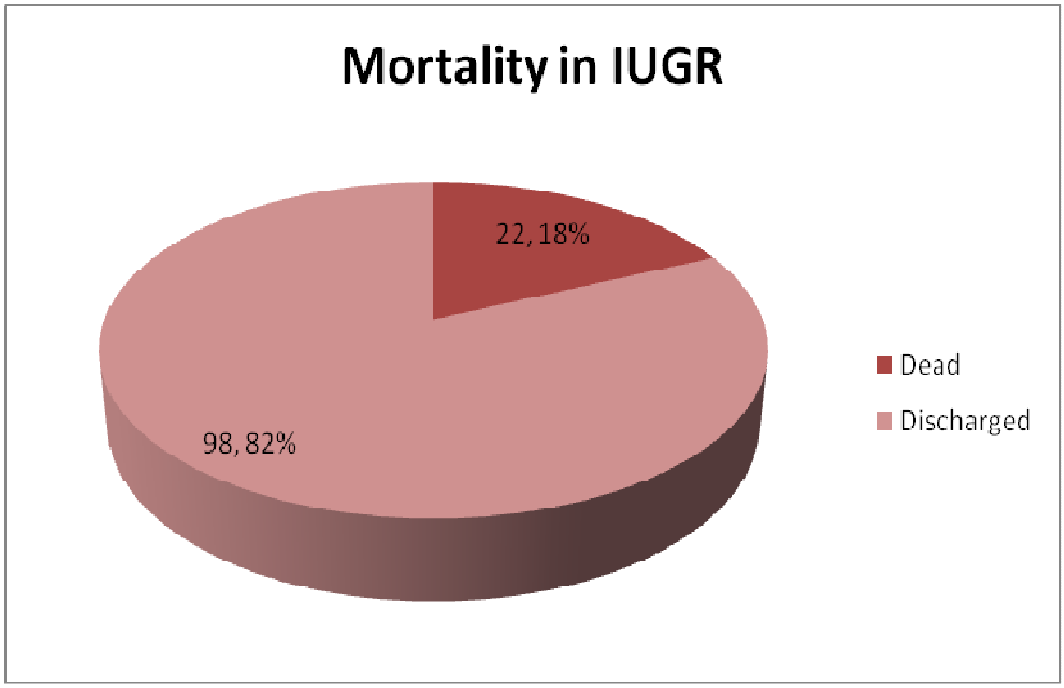

Fig 2.2 Pie diagram showing the Mortality in IUGR

2.4 Outcome of IUGR

Outcome	Number	Percent
Dead	22	18.3
Abnormal Neurological Exam. at Discharge	19	15.3
Good condition at Discharge	79	66.3
Total	120	100

Of the 120 babies 22 (18.3%) have died in the hospital. 19 (15.5%) have been discharged with abnormal neurological examination and 79 (66.3%) have been discharged with Good condition at Discharge condition.

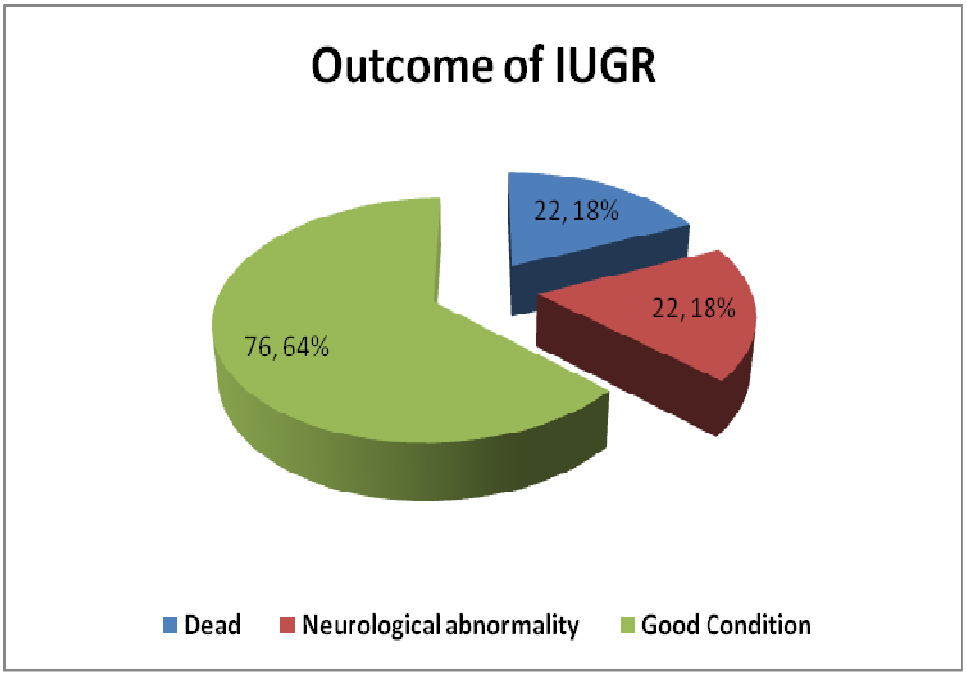

Fig 2.3 Pie diagram showing Outcome of IUGR

2.5 Morbidity pattern and Outcome

Complications	Good condition at Discharge (N=79)	Abnormal N E at Discharge (N=19)	p – Value	Dead (N=22)	p – Value
Metabolic					
Hypoglycemia	52 (65.8%)	8 (42.1%)	0.057	16 (72.7%)	0.541
Hyperglycemia	8 (10.1%)	2 (10.5)	0.959	0 (0.0%)	0.120
Hypocalcaemia	21 (26.6%)	5 (26.3%)	0.981	10 (45.5%)	0.090
Hematological					
Neutropenia	4 (5.1%)	0 (0.0%)	0.317	2 (9.1%)	0.480
Polycythemia	3 (3.8%)	1 (5.3%)	0.772	2 (9.1%)	0.311
Anemia	20 (25.5%)	4 (21.1%)	0.156	4 (18.2%)	0.482
Thrombocytopenia	20 (25.5%)	2 (10.5%)	0.165	8 (36.4%)	0.318
Organ Dysfunction					
Acute Renal Failure	14 (17.7%)	4 (21.1%)	0.736	4 (18.2%)	0.960
Perinatal Asphyxia	27 (34.2%)	13 (68.4%)	**0.006**	14 (63.6%)	**0.013**
Meconium Aspiration	7 (8.9%)	9 (47.4%)	**0.000**	4 (18.2%)	0.215
Pulmonary Hemorrhage	0 (0.0%)	0 (0.0%)	---	6 (27.3%)	**0.000**
Persistent Pulmonary Hypertension	0 (0.0%)	0 (0.0%)	---	4 (18.2%)	**0.000**
Infection/ Others					
Sepsis	24 (30.4%)	8 (42.1%)	0.328	8 (36.4%)	0.594
Meningitis	2 (2.5%)	2 (10.5%)	0.114	2 (9.1%)	0.163
Hypothermia	22 (27.8%)	8 (42.1%)	0.226	4 (18.2%)	0.359
Hyperbillirubinaemia	10 (12.7%)	4 (21.1%)	0.348	6 (27.3%)	0.097

The above table shows the distribution of various morbidity conditions of IUGR babies with their Outcome. Perinatal asphyxia and Meconium Aspiration are significantly associated with abnormal neurological examination at Discharge. Perinatal asphyxia, Pulmonary hemorrhage and Persistent pulmonary hypertension are significantly associated with Death during the hospital stay.

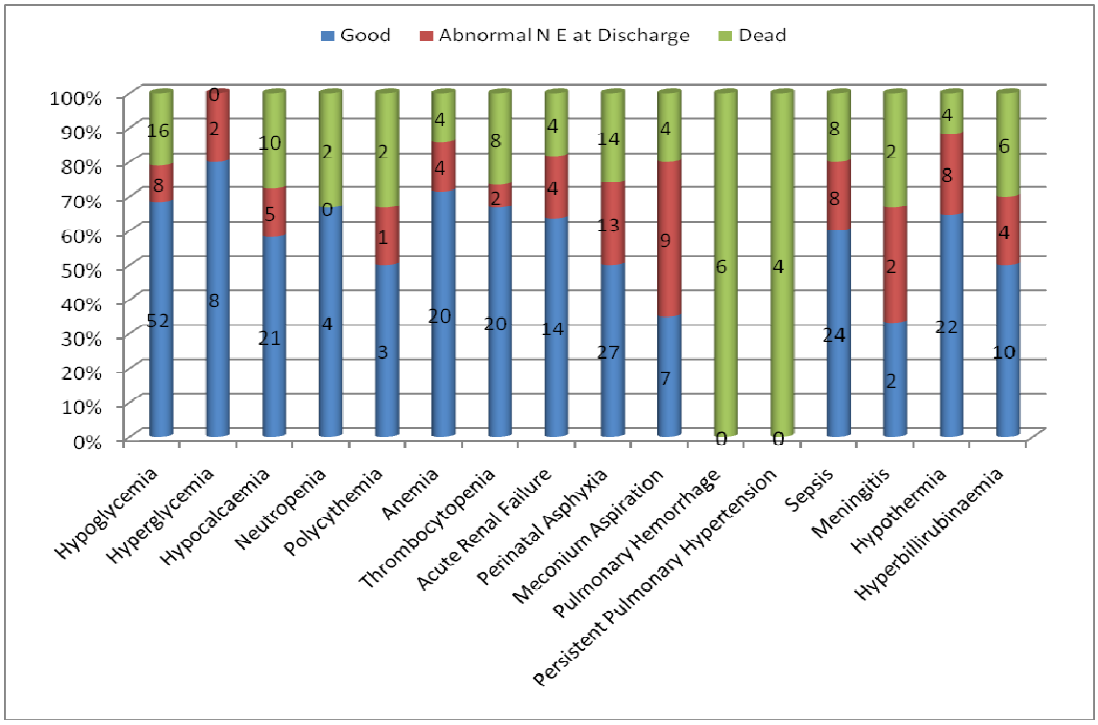

Fig 2.4 showing Morbidity pattern and Outcome

3.0 Distribution of Maternal Risk Factors

3.1 Maternal Risk Factors

Maternal Risk factors	Number	Percent
Anemia	41	34.2
Malnutrition	48	40.0
Multiple Gestations	10	8.3
Heart Disease	8	6.7
Pulmonary Disease	8	6.7
PIH	22	18.3
Diabetes Mellitus	2	1.7
Tobacco Use	4	3.3
Long Infertility	4	3.3
UTI	6	5.0

The above table shows the maternal risk factors associated with IUGR. Malnutrition is the commonest (48 – 40.0%) maternal risk factor. The other commoner are Anemia (41 – 34.2%), PIH (22 – 18.3%) and Multiple Gestations (10 – 8.3%).

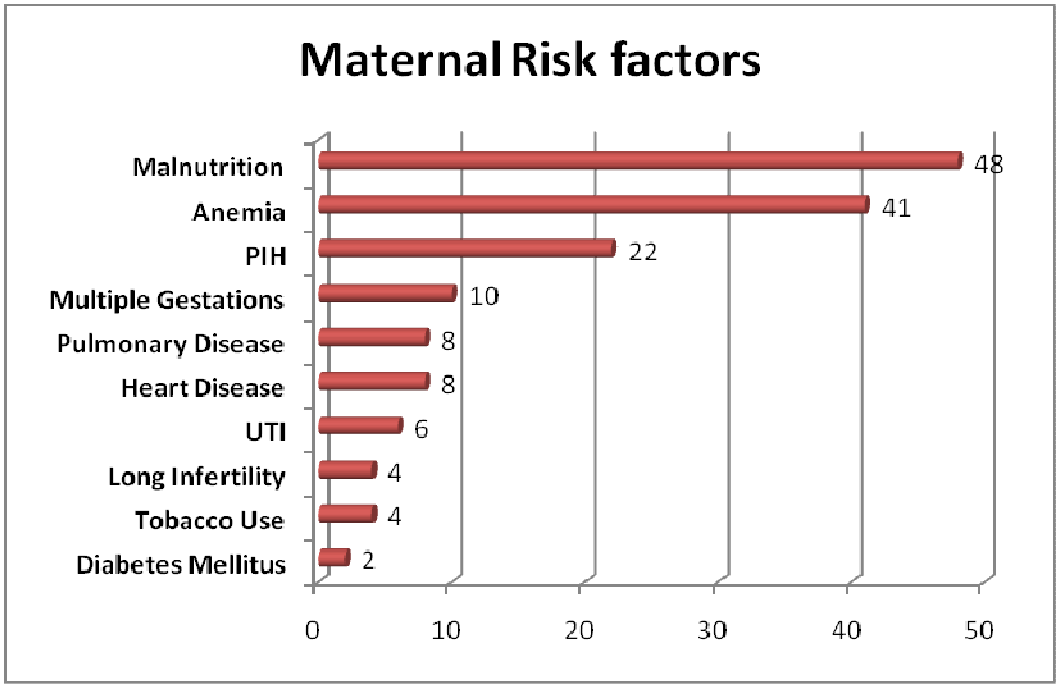

Fig 3.1 Bar Chart showing distribution of Maternal risk factors

3.2 Number of Maternal risk factors

Number of Maternal risk factors	Number	Percentage
No Risk factor	27	22.5
One	56	46.7
Two	23	19.2
Three	12	`10.0
Four	2	1.7
Total	120	100

27 (22.5%) mothers didn't have any specific risk factors. 56 (46.7%) mothers had only one risk factor and 23 (19.2%) had two risk factors. 3 risk factors were present in 12 (10.0%) mothers and only 2 (1.7%) mothers have four risk factors.

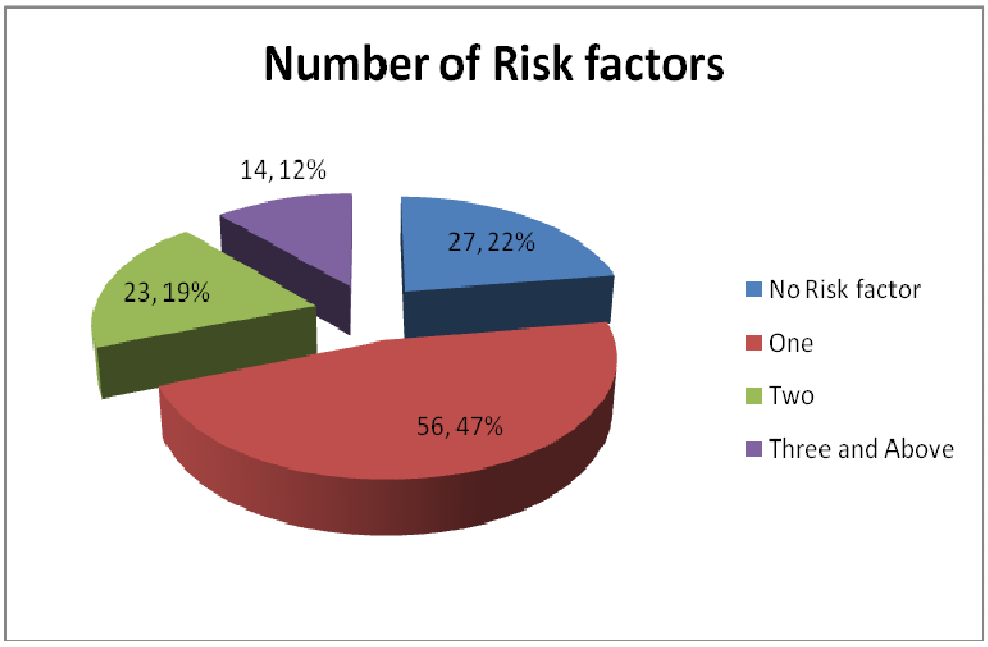

Fig 3.2 Pie diagram showing the number of Maternal Risk factors

4.0 Factors associated with Morbidity and Mortality pattern

4.1.0 Maternal risk factors and Mortality

Maternal Factors	Death N= 22	No Death N= 98	Odds Ratio	95% CI	Chi-2 Value	P-Value
Primi	16 (72.7%)	66 (67.3%)	1.29	0.46 – 3.62	0.240	0.624
Lower Wt. gain	14 (63.6%)	62 (63.3%)	1.02	0.39 – 2.66	0.001	0.974
Malnutrition	15 (68.2%)	33 (33.7%)	4.22	1.57 – 11.4	8.915	**0.003**
Anemia	14 (63.6%)	27 (27.6%)	4.60	1.74 – 12.2	10.40	**0.001**
PIH	6 (27.3%)	16 (16.3%)	1.92	0.65 – 5.66	1.438	0.230
Multiple Gestations	2 (9.1%)	8 (8.2%)	1.13	0.22 – 5.71	0.020	0.887

From the above table, Primi gravida, Lower Wt. gain, Malnutrition, Anemia, PIH and Multiple gestations are the risk factors associated with mortality in IUGR. Among them Malnutrition and Anemia have significant association (p- value < 0.05).

4.1.1 Malnutrition and Outcome

Malnutrition	Dead	Abnormal N E at Discharge	Good condition at Discharge	Total
Present	15 (31.3%)	10 (20.8%)	23 (47.9%)	48 (100%)
Absent	7 (9.7%)	9 (12.5%)	56 (77.8%)	72 (100%)
Total	22 (18.3%)	19 (15.8%)	79 (65.8%)	120 (100%)

Chi^2: 12.444 df: 2 p – Value: **0.002**

Malnutrition is significantly associated with mortality (p- value < 0.05).

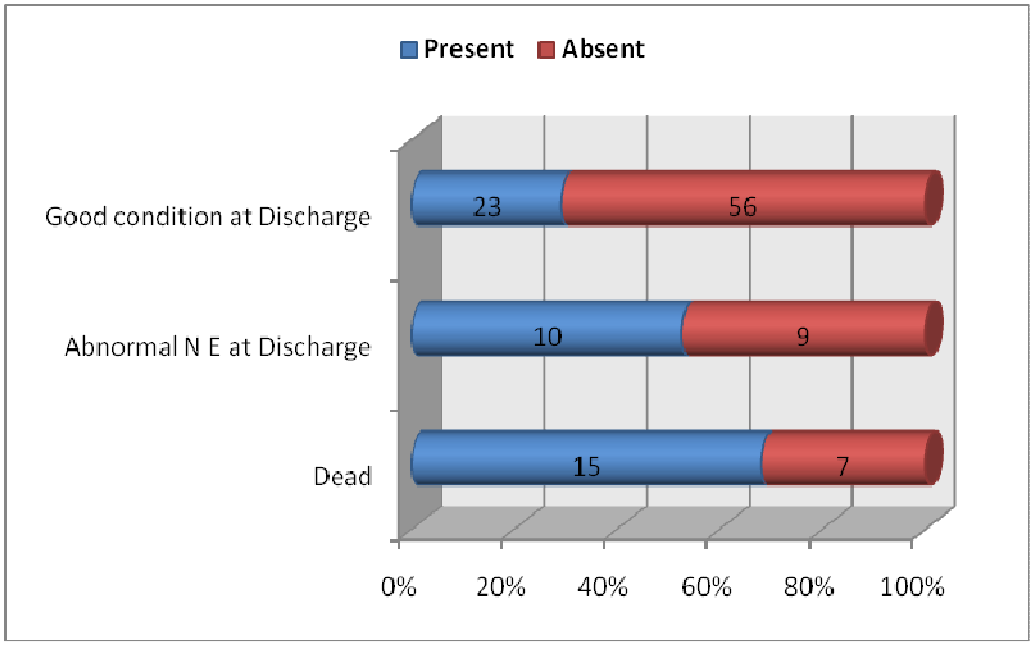

Fig. 4.1 Bar Chart showing Malnutrition and outcome.

4.1.2 Anemia and Outcome

Anemia	Dead	Abnormal N E at Discharge	Good condition at Discharge	Total
Present	14 (34.1%)	5 (12.2%)	22 (53.7%)	41 (100%)
Absent	8 (10.1%)	14 (17.7%)	57 (17.2%)	79 (100%)
Total	22 (18.3%)	19 (15.8%)	79 (65.8%)	120 (100%)

Chi^2 – 10.417 df: 2 p – Value: **0.005**

Anemia is significantly associated with mortality (p- value < 0.05).

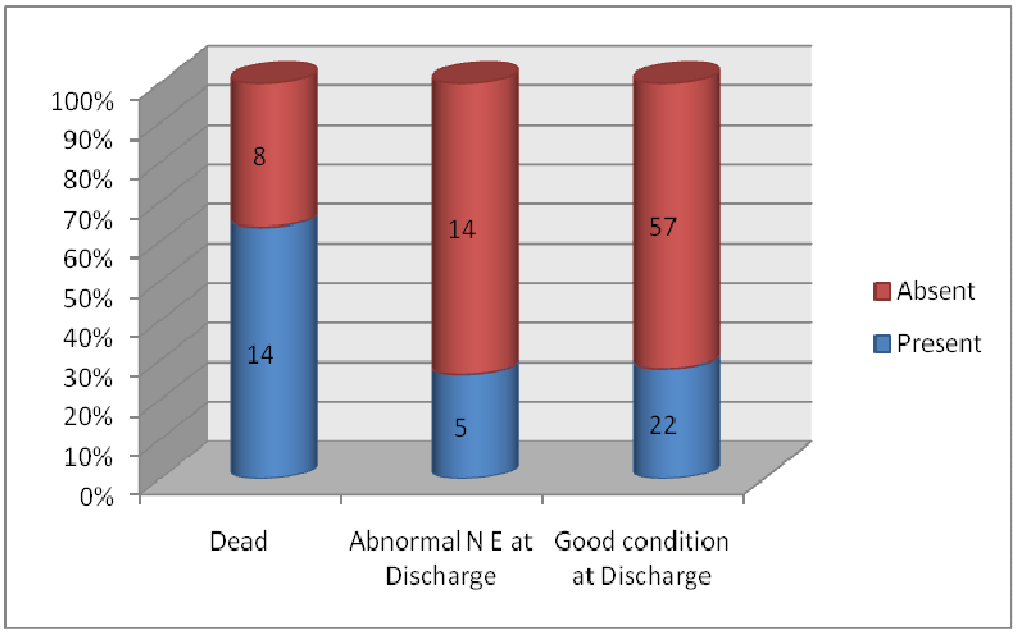

Fig 4.2 Bar Chart showing Anemia and Outcome

4.1.3 Number of Maternal risk factors and Mortality

Number of Maternal risk factors	Dead (N=22)	Alive (N=98)	Total
No Risk factor	6 (27.3%)	21 (21.4%)	27 (22.5%)
One	5 (22.7%)	51 (52.0%)	56 (46.7%)
Two	5 (22.7%)	18 (18.3%)	23 (19.2%)
Three	4 (18.2%)	8 (8.2%)	12 (10.0%)
Four	2 (9.1%)	0 (0.0%)	2 (1.7%)
Total	22 (100%)	98 (100%)	120 (100%)

Chi^2 – 14.762 df: 4 p – Value: **0.005**

The above table shows the relationship with the numbers of risk factors and mortality. There is a statistically significant association that the higher the number of maternal risk factors, higher the mortality (p- value < 0.001).

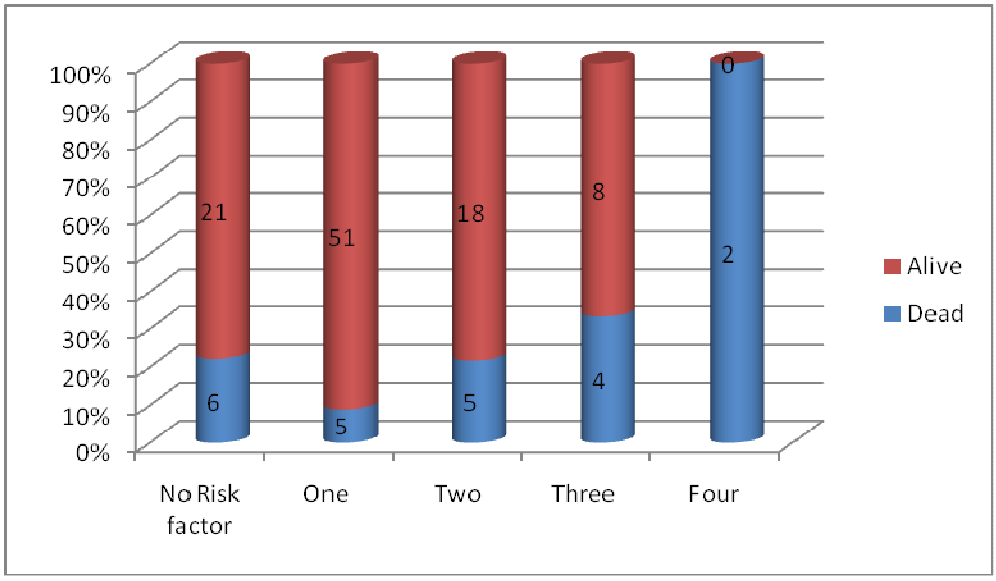

Fig 4.3 Bar Diagam showing Number of Maternal risk factors and Outcome

4.2 Socio Demographic factors and Mortality

Socio Demographic Factors	Death N= 22	No Death N= 98	Odds Ratio	95% CI	Chi-2 Value	P-Value
Lower Age (≤ 25 yrs) (Mean)	14 (63.6%)	40 (40.8%)	2.54	1.12 – 6.61	4.260	**0.042**
Residence -Rural	17 (77.3%)	64 (65.3%)	1.64	0.65 – 4.11	1.172	0.278
Lower Income (≤ Rs. 3000) (Mean)	19 (81.8%)	51 (55.1%)	4.16	1.31 – 13.27	5.343	**0.006**
Lower Education (≤ Primary School)	16 (72.7%)	67 (68.4%)	1.19	0.51 – 2.79	0.160	0.689

The above table shows that the lower Age of the mother and the lower monthly income of the family are significantly associated with mortality in IUGR (*p- value < 0.05*).

4.3.0 Fetal risk factors and Mortality

Fetal Factors	Death N= 22	No Death N= 98	Odds Ratio	95% CI	Chi-2 Value	P-Value
Sex- Male	13 (59.1%)	52 (53.1%)	1.28	0.50 – 3.26	0.263	0.608
Weight ≤ 2 kg	15 (68.9%)	39 (39.8%)	3.24	1.11 – 9.76	5.850	**0.015**
GA - Preterm	8 (36.4%)	14 (14.3%)	3.43	1.22 – 9.67	5.849	**0.016**
Symmetrical IUGR	10 (45.5%)	28 (28.6%)	2.08	0.81 – 5.37	2.367	0.124
Normal Delivery	18 (81.8%)	54 (55.1%)	3.67	1.16 – 11.63	5.343	**0.021**

The above table shows that Weight ≤ 2 kg, Preterm, Normal delivery have the statistically significant association with mortality (*p- value < 0.05*).

4.3.1 Birth Weight and Outcome

Birth Weight	Dead	Abnormal N E at Discharge	Good condition at Discharge	Total
< 1000 gm	6 (100%)	0 (0.0%)	0 (0.0%)	6 (100%)
1000 – 1499 gm	3 (30.0%)	1 (10.0%)	7 (60.0%)	10 (100%)
1500 – 1999 gm	8 (21.1%)	3 (7.9%)	27 (71.0%)	38 (100%)
2000 – 2500 gm	5 (7.5%)	15 (22.8%)	46 (69.7%)	66 (100%)
Total	22 (18.3%)	19 (15.8%)	79 (65.8%)	120 (100%)

Chi^2 – 36.160 df: 6 p – Value: **0.000**

The table shows that lower the weight more associated with Death during hospital and also this is statistically significant (p- value < 0.0001).

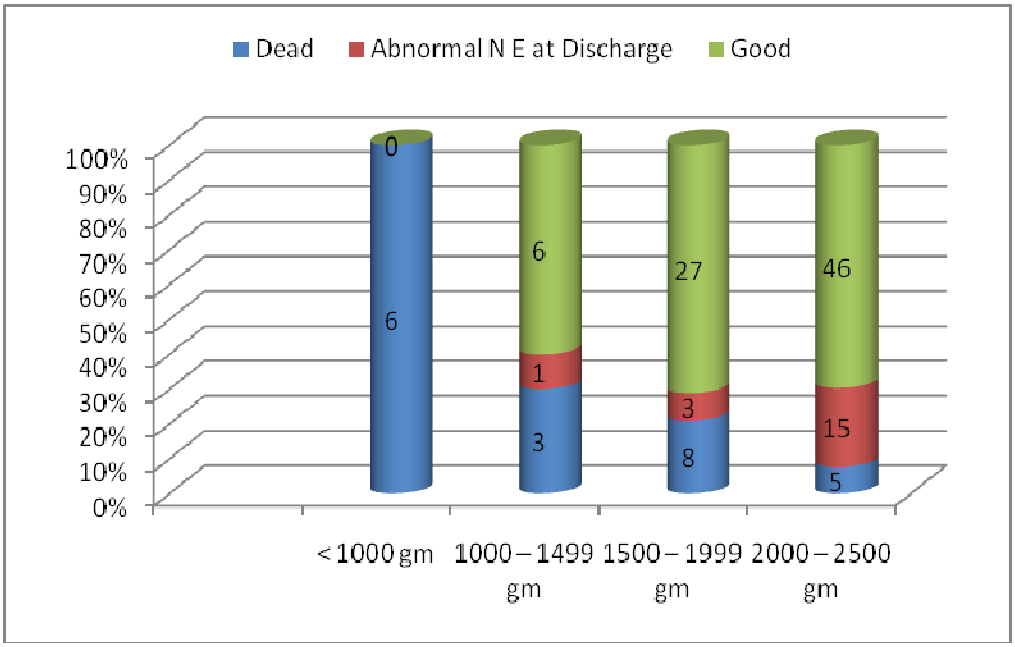

Fig. 4.4 Bar Chart showing Birth weight and Outcome

4.3.2 Gestational Age and Outcome

Gestational Age	Dead	Abnormal N E at Discharge	Good condition at Discharge	Total
< 32 weeks	7 (87.50%)	0 (0.0%)	1 (12.5%)	8 (100%)
33- 37 weeks	6 (20.0%)	2 (6.7%)	22 (73.3%)	30 (100%)
38- 40 weeks	8 (10.8%)	15 (20.3%)	51 (68.9%)	74 (100%)
> 40 weeks	1 (12.5%)	2 (25.0%)	5 (62.5%)	8 (100%)
Total	22 (18.3%)	19 (15.8%)	79 (65.8%)	120 (100%)

Chi^2 – 23.433 df: 6 p – Value: **0.001**

The above table shows that the lower gestational age is significantly associated with higher chance of Death during hospital stay as compared to higher gestational ages (p-value < 0.01).

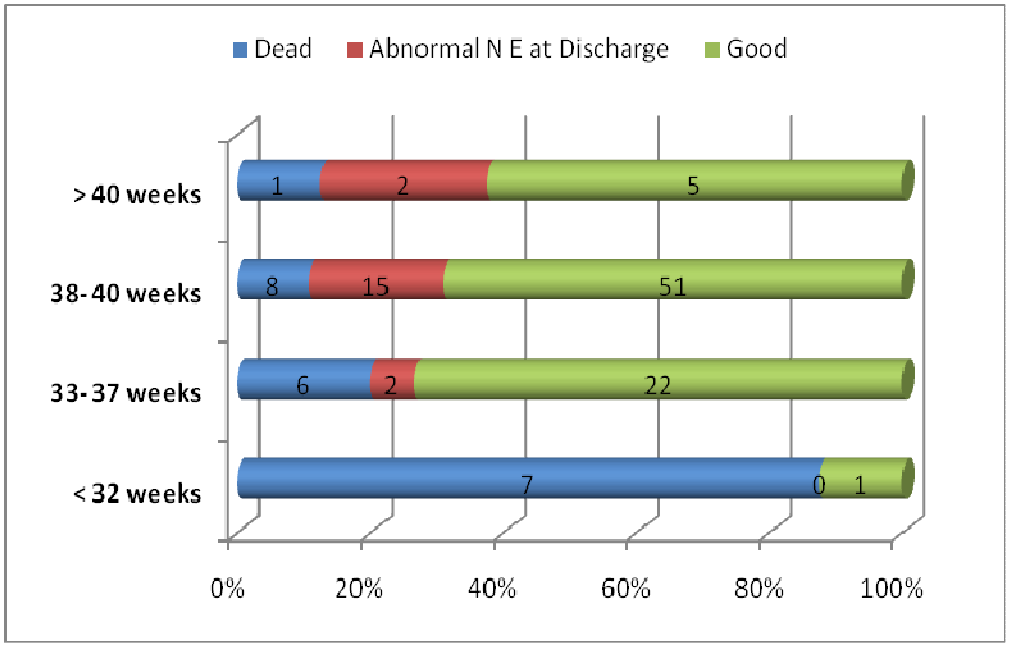

Fig 4.5 Bar chart showing the Gestational age and Outcome.

4.3.3 Mode of Delivery and Outcome

Mode of Delivery	Dead	Abnormal N E at Discharge	Good condition at Discharge	Total
Normal	18 (25.0%)	12 (16.7%)	42 (58.3%)	72 (100%)
Assisted	4 (40.0%)	1 (10.0%)	5 (50.0%)	10 (100%)
LSCS	0 (0.0%)	6 (15.8%)	32 (84.2%)	38 (100%)
Total	22 (18.3%)	19 (15.8%)	79 (65.8%)	120 (100%)

Chi^2 – 14.465 df: 4 p – Value: **0.006**

The above table and the following picture show that Death is significantly associated with Normal delivery than other mode of deliveries (p- value < 0.01).

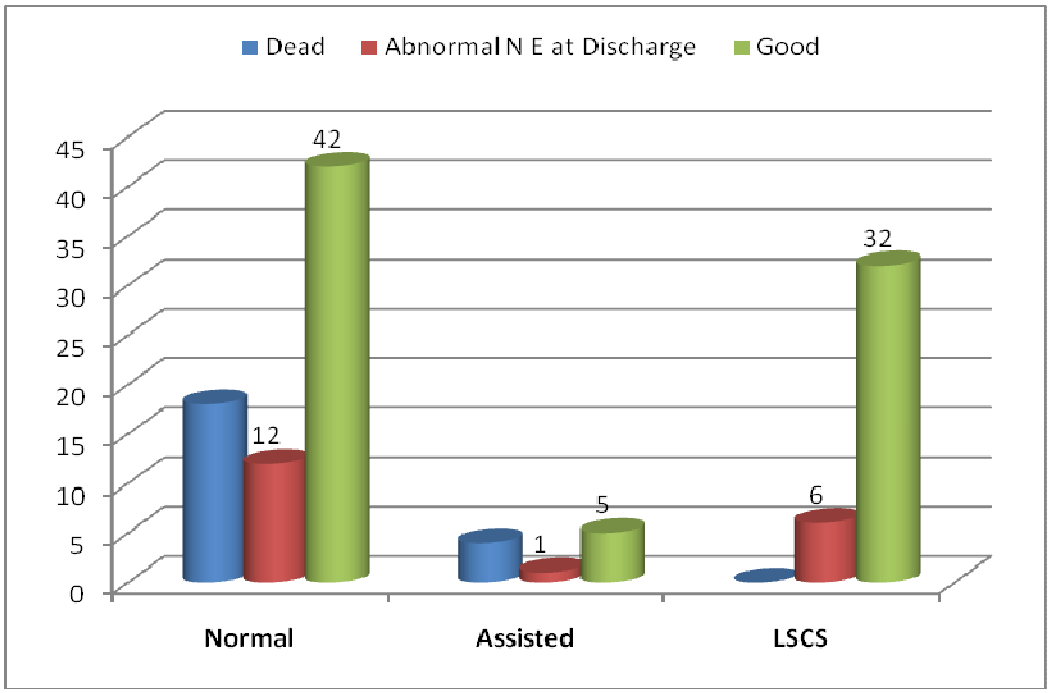

Fig 4.6 Bar Chart showing the Mode of delivery and Outcome

4.4 Perinatal Asphyxia Stages and Outcome (N=54)

HIE STAGE	Dead	Abnormal N E at Discharge	Good condition at Discharge	Total
Stage I	0 (0.0%)	0 (0.0%)	21(100%)	21(100%)
Stage II	5 (25.0%)	9 (45.0%)	6 (30.0)	20 (100%)
Stage III	9 (69.2%)	4 (30.8%)	0 (0.0%)	13 (100%)
Total	14 (25.9%)	13 (24.1%)	27 (50.0%)	54 (100%)

Chi^2: 42.390 df:4 p- value: **0.000**

The above table shows that Higher the HIE stage, higher the mortality in IUGR. This association is also statistically significant (*p- value < 0.001*). In the category of HIE Stage 3, all 4 have abnormal neurological examination, put on anti-epileptic drugs and having poor feeding. In the Stage 2 of 9, 2 are ANE, AED and PF; 7 AED of which 4 had PF.

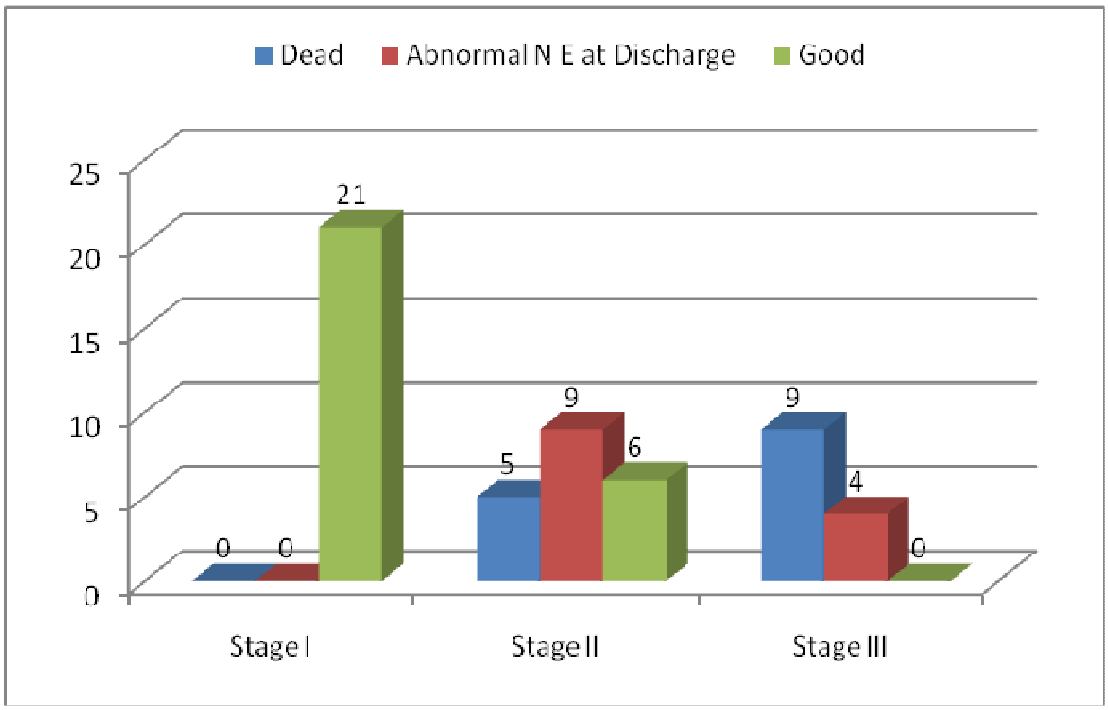

Fig 4.7 Bar Chart showing the HIE Stages and Outcome

7. DISCUSSION

7.1 General characteristics

Of the 120 IUGR babies under the study, 65 (54.2%) are male and 55 (45.8%) are female. Among their respective mothers, 82 (68.3%) mothers are primi and 28 (23.3%) are 2nd gravida mothers. The 3rd gravida mothers are 8 (6.7%) and only 2 (1.7%) are the 4th gravida mothers.

72 (60.0%) have been delivered by normal vaginal delivery and 10 (8.3%) have been delivered by Assisted delivery. 38 (31.7%) have been delivered by Caesarian section. 22 (18.3%) are Preterm babies and 98 (81.7%) are Term babies.

66 (55.0%) are in the birth weight category of 2.0 - 2.5 kg and 38 (31.7%) are in the birth weight category of 1.5 – 2.0 kg. 10 (8.3%) babies are in the category of 1.0 – 1.5 kg and 6 (5.0%) babies are in less than 1.0 kg category. 82 (68.3%) babies were classified as asymmetrical IUGR and 38 (31.7%) babies were classified as symmetrical IUGR as per Ponderal Index.

Of the 120 IUGR babies 22 (18.3%) have died at hospital and 98 (81.7%) have been discharged. Of these 98 babies, 79 (66.3%) have been discharged with good condition and 19 (15.5%) with abnormal neurological examination.

7.2 Morbidity and Mortality Pattern

Regarding the complications, Hypoglycemia (63.3%) and Perinatal Asphyxia (45.0%) are the commonest of the complications observed in this study. Carbohydrate metabolism is seriously disturbed and these infants are highly susceptible to hypoglycemia as the consequence of diminished glycogen reserves and decreased

capacity to gluconeogenesis.[35] IUGR infants frequently do not tolerate labor and vaginal delivery, and signs of fetal distress are common.

Other commoner are Sepsis (33.3%), hypocalcaemia (30.0%), hypothermia (28.3%) and thrombocytopenia (25.0%). Other complications are Hyperglycemia (10 - 8.3%), Neutropenia (6 - 5.0%), Polycythemia (6 - 5.0%), Anemia (24 - 20.0%), Acute Renal Failure (22 - 18.3%), Meconium Aspiration (20 - 16.7%), Pulmonary Hemorrhage (6 - 5.0%), Persistent Pulmonary Hypertension (4 - 3.3%) and Meningitis (6 - 5.0%).

There are totally 22 preterm babies. Among them only 7 (31.8%) babies have Respiratory Distress Syndrome. This is due to as *McIntire DD et al*[51] explained in their study that in IUGR babies, accelerated fetal pulmonary maturation occurs secondary to chronic intra uterine stress.

Perinatal asphyxia and Meconium Aspiration are significantly associated with abnormal neurological examination at Discharge. Perinatal asphyxia, Pulmonary hemorrhage and Persistent pulmonary hypertension are significantly associated with Death during the hospital stay.

7.3 Factors associated with Morbidity and Mortality pattern of IUGR

7.3.1 Maternal factors

Malnutrition is the commonest (48 – 40.0%) maternal risk factor in this study. Malnutrition during uterine growth leads to the onset of stunting which is not completely reversed even with long term exposure to good nutrition.[52] According to Jane Harding[17], fetal nutrition is the end result of a precarious supply chain, of which maternal nutrition and intake during pregnancy is only the starting point. Maternal malnutrition leads to deficient substrate supply to the fetus.

The other commoner maternal risk factors are Anemia (41 – 34.2%), PIH (22 – 18.3%) and Multiple Gestations (10 – 8.3%). In a study done by *Deborah Watson Jones et al*[64], Anemia was observed in women who had adverse birth outcomes, 33.8% had moderate to severe anemia. PIH results in decreased utero placental bold flow which results in impaired delivery of oxygen and other essential nutrients which in turn limit organ growth and musculo skeletal maturation.[53] Impaired growth results from failure to provide optimal nutrition for more than one fetus in utero and the smaller twin has decreased nutrient delivery. Others factors found in this study are Heart Disease (8 - 6.7%), Pulmonary Disease (8 - 6.7%), Diabetes Mellitus (2 -1.7%), Tobacco Use (4- 3.3%), Long Infertility (4 - 3.3) and UTI (6- 5.0%).

27 (22.5%) mothers didn't have any specific risk factors. 56 (46.7%) mothers had only one risk factor and 23 (19.2%) had two risk factors. 3 risk factors were present in 12 (10.0%) mothers and only 2 (1.7%) mothers have four risk factors. Table 4.1.3 shows the relationship with the numbers of risk factors and mortality. There is a statistically significant association that the higher the number of maternal risk factors, higher the mortality (p- value < 0.001)

Primi gravida, Lower Wt. gain, Malnutrition, Anemia, PIH and Multiple gestations are the risk factors associated with mortality in IUGR (Table 4.1). Among them Malnutrition and Anemia have significant association (p- value < 0.05). *Gawande et al*[54] found in their study that primi gravida is more common in IUGR and significantly associated with morbidity. *Bakketeig LS et al*[55] in their study proved that Lower weight gain is one of the important factors associated with IUGR. Maternal malnutrition and Anemia in particular has been established as a critical factor behind

IUGR problem in India in other studies done by *Acharya D et al*[56] at Karnataka, *Ferriera AMA et al*[57] at and CSSM review report.[58]

4.3.2 Sociodemographic factors

The lower Age of the mother and the lower monthly income of the family are significantly associated with mortality in IUGR (*p- value < 0.05*) (Table 4.2). Lower maternal age and its relationship with mortality in IUGR has been proved in the study done by *Gawande et al*[54]. Families with IUGR infants tend to be more disadvantaged in income, housing, parental education etc. than families of appropriately grown infants.[59]

4.3.3 Fetal factors

Weight ≤ 2 kg, Preterm and Normal delivery have the statistically significant association with mortality (*p- value < 0.05*) (Table 4.3). *Hack M, Fanaroff AA*[60] in their study on outcome of extremely low birth weight and gestational age IUGR babies found that lower birth weight and lower gestational age are significantly associated with morbidity and mortality. It is consistent with study done by *McIntire DD et al*.[51] Table 4.3.1 details how the birth weight is associated with mortality during hospital.

Table 4.3.2 depicts how lower gestational age is significantly associated with higher chance of Death during hospital stay as compared to higher gestational ages. *Garite TJ et al*[61] found that preterm infants have higher incidence of abnormalities than the general population because they are subjected to the risk of prematurity in addition to the risks of IUGR. IUGR infants delivered before 28 – 30 weeks had worse outcomes.

In this study also, of the 8 Infants born before 32 weeks, 7 have died. This is statistically significant (p- value < 0.01).

Morbidity in IUGR is significantly associated with Normal delivery (Table 4.3.3) than other mode of deliveries (p- value < 0.01). IUGR babies frequently have birth asphyxia as they tolerate the stress of labour poorly. This is consistent with other studies by *Hawdon JM et al*[62] and *Pérez-Escamilla R et al*[63]. This may be due to labour is stressful for IUGR fetuses. Skilled resuscitation should be available because perinatal depression is common. The availability of pediatrician for the skillful resuscitation also may contribute for the favorable outcome of IUGR in assisted delivery / caesarian section.

8. CONCLUSIONS

The following are the observations and conclusions of the study.

1. In this study, of the 120 IUGR babies 65 (54.2%) are male and 55 (45.8%) are female.

2. According to Ponderal Index 82 (68.3%) babies are asymmetrical IUGR and 38 (31.7%) are symmetrical IUGR. Ratio Asymmetrical: symmetrical = 2.15:1. Symmetrical IUGR is 2.08 times more risk of having mortality as compared to asymmetrical IUGR.

3. Hypoglycemia (63.3%) and Perinatal Asphyxia (45.0%) are the commonest complications of IUGR. Other commoner are Sepsis (33.3%), hypocalcaemia (30.0%), hypothermia (28.3%) and thrombocytopenia (25.0%).

4. Of the 120 babies, 22 (18.3%) died at hospital and 98 (81.7%) have been discharged. Of these 98 babies, 79 (66.3%) have been discharged in good condition and 19 (15.5%) with abnormal neurological examination.

5. Perinatal asphyxia and Meconium Aspiration are significantly associated with abnormal neurological examination at Discharge. Perinatal asphyxia, Pulmonary hemorrhage and Persistent pulmonary hypertension are significantly associated with Death during the hospital stay.

6. Malnutrition is the commonest (40.0%) maternal risk factor in this study. The other commoner are Anemia (34.2%), PIH (18.3%) and Multiple Gestations (8.3%).

7. 73 (77.5%) mothers had one or more risk factors. There is a statistically significant association that the higher the number of maternal risk factors, higher the mortality in IUGR.

8. Malnutrition and Anemia are the statistically significant maternal factors associated with mortality in IUGR.

9. Lower age of the mother and the lower monthly income of the family are significantly associated with mortality.

10. Lower gestational age, Normal delivery and Lower weight of the baby are the statistically significant fetal risk factors associated with mortality.

9. RECOMMENDATIONS

From the conclusions arrived at this study, the following recommendations can be made to prevent the incidence and the complications in IUGR.

1. Hypoglycemia, hypocalcaemia and hypothermia are the common treatable complications in this study which can be easily identified and treated. So in IUGR babies it is important to anticipate these conditions and treat appropriately to prevent further morbidity and mortality.

2. Perinatal asphyxia is the second most common complication observed in this study which is significantly associated with morbidity and mortality. Hence anticipating perinatal asphyxia, effective neonatal resuscitation measures should be made available for every IUGR delivery.

3. Malnutrition and Anemia are the most common maternal risk factors in this study and significantly associated with mortality in IUGR. As these are the preventable risk factors, the nutritional status of the prospective mothers should be given utmost importance.

10. LIMITATIONS

Placental factors significantly contribute to IUGR, but only non - Placental factors associated with IUGR have been considered in this study due to the inclusion of out born babies also.

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ANNEXURE: 1

PROFORMA – IUGR STUDY

IP No : S. No :

Name : Sex : M / F

DOB : Time:

Age of Mother: Yrs. G: P: L: A:

Education : Illiterate/ Primary/Middle/High School/ HSS /Diploma / Graduate

Occupation : House-wife / Coolie / Farmer / Employed / Business /

Husband's Occupation: Coolie / Farmer / Employed / Business /

Total monthly Income:

Religion : Hindu / Christian / Muslim / Others

Gestational age : wks. LMP: EDD:

Prepregnancy Wt : Kgs. Height : Cm

Wt gain during pregnancy : Kgs.

Hemoglobin : gm%

Mode of Delivery : Normal Vaginal / Assisted / Caesarean

Risk Factors in Mother:

Malnutrition		Pregnancy induced Hypertension	
Multiple Gestations		Diabetes Mellitus	
Uterine Anomalies		Long Infertility	
Anemia		Thrombotic Disease	
Heart Disease (RHD, CHD)		Collagen vascular Disease	
Renal Disease		Tobacco/Cocaine use	
Pulmonary disease (Bronchial Asthma, COPD)		UTI	

CLINICAL EXAMINATION:

Birth Weight : APGAR Score: 1 Min: 5 Min:

HC: CC: Length:

Ponderal Index: CANS Score:

Cry: Fair/ Weak / Absent Activity: Fair / Weak / Absent

Colour: Pink / Cyanosed / Plethoric

Temperature: Normothermic / Hypothermic / Hyperthermic

RS: CVS: Abdomen:

LABORATORY INVESTIGATIONS:

1) CBC - Hb, PCV, TC, DC, Platelet Count, ESR.
2) Blood sugar
3) Blood Urea

4) Serum Creatinine
5) Serum Electrolytes
6) Serum calcium
7) Sepsis Screening (in probable sepsis)
    a. TC
    b. Micro ESR,
    c. Peripheral smear for band forms
    d. Toxic granules
    e. Blood culture and sensitivity
    f. CSF Analysis
    g. CSF culture and sensitivity
    h. CXR.

COMPLICATIONS:

Perinatal depression		Hypocalcemia	
Meconium aspiration		Polycythemia	
Pulmonary Hemorrhage		Thrombocytopenia	
Persistent Pulmonary hypertension		Hyperbilirubinemia	
Hypothermia		Sepsis	

OUTCOME: Dead / Abnormal neurological examination at Discharge/ Good condition at Discharge.

ANNEXURE: 2

INTRA UTERINE GROWTH CHARTS – LUBCHENCO

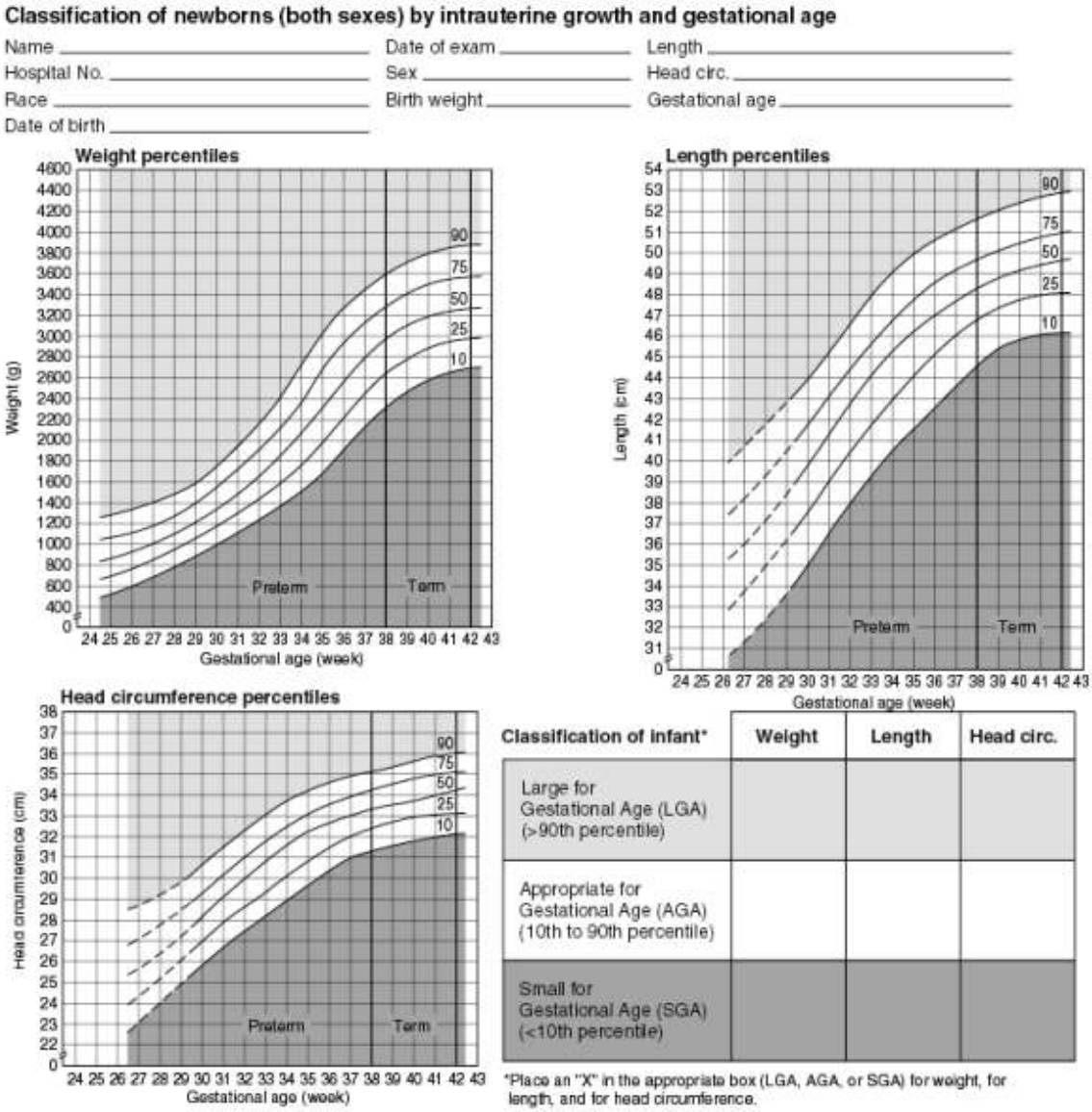

FIGURE 3-2. Classification of newborns (both sexes) by intrauterine growth and gestational age. *(Reproduced, with permission, from Battaglia FC, Lubchenco LO: A practical classification for newborn infants by weight and gestational age.* J Pediatr *1967;71:159; and Lubchenco LO et al: Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks.* Pediatrics *1966;37:403. Courtesy of Ross Laboratories, Columbus, Ohio 43216.)*

ANNEXURE: 3

ASSESSMENT OF GESTATIONAL AGE - NEW BALLARD'S SCORING

MATURATIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballard Score)

Name _____ Date/Time of birth _____ Sex _____ **SCORE**

Hospital No. _____ Date/Time of exam _____ Birth weight _____ Neuromuscular _____

Race _____ Age when examined _____ Length _____ Physical _____

Apgar score: 1 minute _____ 5 minutes _____ 10 minutes _____ Head circ. _____ Total _____

Examiner _____

Neuromuscular maturity

Neuromuscular maturity sign	Score							Record score here
	−1	0	1	2	3	4	5	
Posture								
Square window (wrist)	>90°	90°	60°	45°	30°			
Arm recoil		180°	140° to 180°	110° to 140°	90° to 110°	<90°		
Popliteal angle	180°	160°	140°	120°	100°	90°	<90°	
Scarf sign								
Heel to ear								
							Total neuromuscular maturity score	

Maturity rating

Score	Weeks
−10	20
−5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Physical maturity

Physical maturity sign	Score							Record score here
	−1	0	1	2	3	4	5	
Skin	sticky friable transparent	gelatinous red translucent	smooth pink visible veins	superficial peeling &/or rash, few veins	cracking pale areas rare veins	parchment deep cracking no vessels	leathery cracked wrinkled	
Lanugo	none	sparse	abundant	thinning	bald areas	mostly bald		
Plantar surface	heel-toe 40–50 mm: −1 <40 mm: −2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
Breast	imperceptible	barely perceptible	flat areola no bud	stippled areola 1–2 mm bud	raised areola 3–4 mm bud	full areola 5–10 mm bud		
Eye/ear	lids fused loosely: −1 tightly: −2	lids open pinna flat stays folded	sl. curved pinna; soft slow recoil	well curved pinna; soft but ready recoil	formed and firm, instant recoil	thick cartilage ear stiff		
Genitals (male)	scrotum flat, smooth	scrotum empty, faint rugae	testes in upper canal rare rugae	testes descending few rugae	testes down good rugae	testes pendulous deep rugae		
Genitals (female)	clitoris prominent & labia flat	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large minora small	majora cover clitoris & minora		
							Total physical maturity score	

Gestational age (weeks)

By dates _____

By ultrasound _____

By exam _____

FIGURE 3-1. Maturational assessment of gestational age (New Ballard Score). *(Reproduced, with permission, from Ballard JL et al: New Ballard Score, expanded to include extremely premature infants.* J Pediatr *1991;119:417.)*

ANNEXURE: 4

SARNAT AND SARNAT STAGING OF HYPOXIC ISCHEMIC ENCEPHALOPATHY

	State 1	Stage 2	Stage 3
Level of Consciousness	Hyperalert	Lethargic or obtunded	Stuporous
Neuromuscular Control			
Muscle tone	Normal	Mild hypotonia	Flaccid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
Stretch reflexes	Overactive	Overactive	Decreased or absent
Segmental myoclonus	Present	Present	Absent
Complex Reflexes			
Suck	Weak	Weak or absent	Absent
Moro	Strong; low threshold	Weak; incomplete; high threshold	Absent
Oculovestibular	Normal	Overactive	Weak or absent
Tonic neck	Slight	Strong	Absent
Autonomic Function	Generalized sympathetic	Generalized parasympathetic	Both systems depressed
Pupils	Mydriasis	Miosis	Variable; often unequal; poor light reflex
Heart Rate	Tachycardia	Bradycardia	Variable
Bronchial and Salivary Secretions	Sparse	Profuse	Variable
GI Motility	Normal or decreased	Increased; diarrhea	Variable
Seizures	None	Common; focal or multifocal	Uncommon (excluding decerebration)
EEG Findings	Normal (awake)	Early: low-voltage continuous delta and theta Later: periodic pattern (awake) Seizures: focal 1-to 1-Hz spike-and-wave	Early: periodic pattern with Isopotential phases Later: totally isopotential
Duration	1-3 days	2-14	Hours to weeks

ANNEXURE: 5

ABNORMAL NEUROLOGICAL EXAMINATION - Amiel Tison angles

	6 months 28 weeks	6½ months 30 weeks	7 months 32 weeks	7½ months 34 weeks	8 months 36 weeks	8½ months 38 weeks	9 months 40 weeks
1. POSTURE	Completely hypotonic	Beginning of flexion of thigh at hip	Stronger flexion	Frog-like attitude	Flexion of the four limbs	Hypertonic	Very hypertonic
2. HEEL TO EAR MANOEUVRE							
3. POPLITEAL ANGLE	150°		110°	100°	100°	90°	80°
4. DORSI-FLEXION ANGLE OF FOOT			40-50°		40-50°		Premature reached 40 wk. 40° Full term
5. 'SCARF' SIGN	'Scarf' sign complete with no resistance		'Scarf' sign more limited		Elbow slightly passes midline		Elbow almost reaches midline
6. RETURN TO FLEXION OF FOREARM	Upper limbs very hypotonic lying in extension			Flexion of forearms begins to appear, but very weak	Strong 'return to flexion'. Flexion tone inhibited if forearm maintained 30 sec. in extension	Strong 'return to flexion' Forearm returns very promptly to flexion after being extended for 30 sec.	

FIG. 1.—*Passive tone. Increase of tone with maturity illustrated by means of 6 clinical tests.*

	6 months 28 weeks	6½ months 30 weeks	7 months 32 weeks	7½ months 34 weeks	8 months 36 weeks	8½ months 38 weeks	9 months 40 weeks
1. LOWER EXTREMITY	—	Beginning of extension of lower leg on thigh upon stimulation of soles in lying position	Good support when standing up but very briefly (see illustration below)	Excellent righting reaction of leg →	→	→	
2. TRUNK	—	—	—	± transitory	Good righting of trunk with infant held in vertical suspension (see illustration below)	Good righting of trunk with infant held in walking position (see illustration below)	
3. NECK EXTENSORS Baby pulled backward from sitting position	—	—	Head begins to right itself with great difficulty	Still difficult and incomplete	Good righting but cannot hold it	Begins to maintain head which doesn't fall back for few seconds	Keeps head in line with trunk for more than a few seconds
4. NECK FLEXORS Baby pulled to sitting position from supine	— Head pendulant	— Head pendulant	Contraction of muscles is visible but no movement of head	Head begins to right itself but still hanging back at end of movement	At first head is hanging back, then with sudden movement head goes forward onto chest	Head begins to follow trunk, keeps in line for few seconds in upright position	Difference between Extensors and Flexors has diminished (see illustration below)
			Straightening of legs 		Straightening of trunk  Stimulation		Straightening of head and trunk together 

FIG. 2.—*Active tone. Increase of tone with maturity illustrated by means of 4 tests of righting reactions.*

	6 months 28 weeks	6½ months 30 weeks	7 months 32 weeks	7½ months 34 weeks	8 months 36 weeks	8½ months 38 weeks	9 months 40 weeks
1. SUCKING REFLEX	Weak and not really synchronized with deglutition		Stronger and synchronized with deglutition	Perfect →	→	→	
2. ROOTING REFLEX	Long latency period. Response is slow and imperfect		Complete and more rapid. Hand-to-mouth attraction established	Brisk Complete → Durable	→	→	
3. GRASP REFLEX	Finger grasp is good and reaction spreads up whole upper limb but not strong enough to lift infant up off bed		Stronger	Stronger	The reaction of upper limb is strong enough to lift infant up off bed →	→	
4. MORO REFLEX	Weak, obtained just once, and not elicited every time		Complete reflex →	→	→	→	
5. CROSSED EXTENSION	Flexion and extension in a random pattern, purposeless reaction		Extension but no adduction	Still incomplete	Good response with :- 1. Extension 2. Adduction → 3. Fanning of the toes	→	
6. AUTOMATIC WALKING	—	—	Begins tip-toeing with good support on sole and a righting reaction of legs for a few seconds	Pretty good Very fast Tip-toeing		• A premature who has reached 40 weeks. Walks in a toe-heel progression or tip-toes • A full-term new born of 40 weeks. Walks in a heel-toe progression on whole sole of foot	

FIG. 3.—*Reflex. Development of reflex activity with maturity, illustrated for sucking, rooting, grasp, Moro, crossed extension, and automatic walking reflexes.*